# COMBINED Nd YAG LASER AND EXTERNAL BEAM RADIOTHERAPY FOR PALLIATION IN GASTROINTESTINAL CANCER

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**For my mother Jean who sadly died of cancer on 14th April 1993**

## ABSTRACT

The Nd YAG laser offers rapid relief of symptoms advanced gastrointestinal cancers but deep tumour is inaccessible. External beam radiotherapy alone can be effectively used to treat all local tumour but its effect is delayed and effective recanalisation is often not achieved. There is very little data on how these treatments can best be combined to achieve the optimum clinical result. This thesis reports a series of studies which focus on the combination of endoscopic laser therapy and external beam radiotherapy for palliation of GI cancers.

Laser is effective in palliation of dysphagia in oesophageal cancer but regular repeat treatments are required to maintain symptomatic relief. We have studied the additional use of external beam radiotherapy to reduce frequency of follow up treatments in this group and have identified patients most likely to benefit. We have also studied the effect on quality of life and cost of the additional radiotherapy in patients undergoing laser treatment.

The use of external beam radiotherapy in patients with rectal cancer undergoing laser has been studied. This approach reduces the need for follow up procedures more dramatically than with oesophageal cancers.

The role of endoprostheses in combination with laser and radiotherapy for oesophageal cancer is assessed. Patients with late complications such as fistulae and perforation are probably seen more commonly after laser/radiotherapy combinations. The use of cuffed tubes in this group is described. Standard oesophageal prostheses are useful later in palliation when laser is no longer effective. Tube overgrowth can subsequently present a problem in such patients, but is usually controllable with laser recanalisation.

Conclusion: Laser has an important role in endoscopic palliation of advanced gastrointestinal cancers which is complementary to radiotherapy and intubation.

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## ABBREVIATIONS

| | |
|---|---|
| DCI | Dysphagia controlled interval |
| DXRT | Deep external beam radiotherapy |
| LASA | Linear analogue self assessment |
| MP | Monopolar electrocoagulation |
| Nd YAG | Neodymium Yttrium Aluminium Garnet |
| QL-index | Quality of life index (Spitzer 1981) |
| UCH | University College Hospital |

# CHAPTER 1

## BACKGROUND TO LASER ENDOSCOPY

### 1.1 The history of cautery

The application of heat for cauterization of tumours is ancient, the oldest reference being in the Edwin Smith surgical Papyrus which has been carbon dated to 1700 b.c. The original manuscript was probably produced 1000 years earlier. At that time the Egyptians used the hot iron for treatment of breast cancers. References to cautery for tumour destroying properties can be found again from the 6th century onwards but the technique did not advance until the 1940's when high frequency diathermy was introduced. Direct application of heat by a pre-heated iron instrument was replaced by the direct generation of heat by electric current. It was not until the 1970's that probes which could be introduced either along side an endoscope or down the instrument channel opened up the gastrointestinal tract for electrocoagulation. At about the same time fibres became available which would allow transmission of laser light and thus both endoscopic electrocoagulation and laser therapy was possible.

### 1.2 Tissue effects of heat

Raising the temperature of living tissue to around 60 degrees Centigrade results in desiccation, contraction and protein coagulation, at 100 degrees Centigrade water boils causing cells to explode and at higher temperatures the tissue becomes carbonized and subsequently Vapourises (Cummings 1983). Coagulation is an irreversible denaturation or conformational change of structural proteins and enzymes. It is readily observed macroscopically as whitening of tissue. A detailed histological study of the coagulative change produced by the Nd YAG laser in dog stomach (Kelly 1983) showed initial hyperaemia and oedema followed by thermal contraction with larger amounts of energy. Contraction was thought to be the initial mechanism of haemostasis rather than thrombus formation within vessels which only occurred as a secondary phenomenon. There are several endoscopic devices designed to induce coagulation of tissue but vaporisation can only be safely achieved with the non-contact technique using laser light.

## 1.3 Endoscopic thermal methods

### 1.3.1 Monopolar electrocoagulation

Diathermy is a crude form of monopolar electrocoagulation. An electric current is passed through tissue from an electrode (in this case diathermy forceps) to a metal plate usually attached to the patients leg, this causes heat generation within the tissue. The current is rapidly alternating preventing depolarisation of cells which would occur with a direct current. Current density and thus heating is maximal at the point where the electrode touches tissue and the effect rapidly falls off with distance from the electrode as the current is distributed through increasing volumes of tissue. At open operation quite extensive damage occurs to the tissue adjacent to the point of diathermy which could be dangerous in a thin walled organ.

The simplest endoscopic device consists of a narrow electrode which can be passed down the biopsy channel of an endoscope and pressed against the tissue to be coagulated. It is connected to an electrosurgical generator and a radiofrequency current (> 300,000Hz) is passed between the electrode and a plate strapped to the patients leg. The inactivated probe is applied and then activated, a pre set quantity of energy being delivered and the procedure is then repeated at multiple sites. Good contact between the probe and tissue is essential for the passage of current and this results in adherence to coagulated tissue. The monopolar probe is thus difficult to use in bleeding because the coagulum is often torn of with removal of the probe. To overcome this problem 'liquid' electrodes were developed which use water or saline between the electrode and tissue. This technique, known as 'wet' electrocoagulation, gives better electrical contact and minimises tissue adherence. Another problem with monopolar probes is the large number of parameters affecting the extent of coagulation. The distance between the ground plate and probe varies between individuals as does the electrical conductivity of the tissue. Most importantly the contact surface between probe and tissue varies. The current density is therefore unpredictable and the risk of excessive tissue damage leading to perforation has limited clinical use. Treatment of rectal cancer is however safe as the rectum is retroperitoneal and thus full thickness damage or small perforations are unlikely to have important clinical consequences. Most authors advise general or caudal anaesthesia and treatment is applied via an operating sigmoidoscope. The treatment technique itself varies between centres. An electrocoagulator with a spherical electrode 4 mm in diameter at the tip is commonly used but a needle point electrode which will induce deeper necrosis is an alternative. The sphere is applied to the tumour to be treated and electric current is applied for a few seconds until the tissue treated begins to boil. Fulguration (holding the tip of the electrode over the tumour and destroying the surface by sparking) is avoided by most groups. This practice causes carbonization of the surface and tissue damage is superficial. Some authors treat the tumour surface only once on each occasion (Hoekstra 1985) but others (Madden 1983) prefer to clear the coagulum and retreat up to 5 or 6 times at the same session until all tumour has been coagulated, often treating down to the extrarectal fat.

Loop diathermy or endoscopic transanal resection of rectal cancer (ETAR) can be achieved with a urological resectoscope which is a monopolar probe in the form of a 'loop'. This technique is very similar to transurethral resection of the prostate. Restriction to oral fluids for 24 hours prior to operation and a phosphate enema is all the preparation that is required. The procedure is performed under spinal or general anaesthetic in the lithotomy position. The resectoscope is inserted and the resection performed with a continuous infusion of 1.5% glycine. Resection is deeper , the limits being judged by the appearance of circular or longitudinal muscle fibres.

### 1.3.2 Bipolar electrocoagulation

These probes were introduced in an attempt to minimise the risk of full thickness damage seen with monopolar probes. The positive and negative poles are located close to each other on the operating probe. This dispenses with the need for a plate or dispersive electrode. Multiple electrodes can be incorporated into a single device. There are usually 2 or 3 pairs (BICAP) of bipolar electrodes allowing diathermy with tip angulation. The probes come in various sizes early probes being 2.3mm diameter and later ones 3.2mm or 3.4mm diameter, with a central irrigation channel. Early power sources deliver 25 watts, the later units 50 watts. The technique for coagulation is identical to that employed with the monopolar and heater probes. Large tumour probes can be inserted alongside the endoscope.

### 1.3.3 Heater probe

The heater probe was developed in 1978 (Protell). It was designed to apply pressure and heat simultaneously to a bleeding vessel. The probe comprises a hollow aluminium cylinder with an inner heater coil and an outer coating of non stick teflon. It also contains a separate thermocouple element in the tip to measure its temperature and can be heated to a maximum of 250 degrees C. The probe temperature is maintained until a preset amount of energy is delivered. There is also a proximal irrigation port to allow washing of the target even when the probe is forcibly applied to tissue. The technique was not designed for use in cancers although it could potentially be used for this application.

## 1.4 The development of lasers

The development of lasers was dependent on our modern understanding of the dual nature of the physical properties of light and atomic structure.

### 1.4.1 Light Theories

In the 17th Century these properties were explained by two different theories. Isaac Newton postulated a corpuscular theory which envisaged light as a stream of particles and Robert Hooke and Christian Huygens considered light as a wave propagating through an all-pervading elastic medium they called the 'aether'. Newton felt that the wave theory could explain neither the rectilinear propagation of light nor polarisation and his view prevailed until the early 19th Century. Young and Fresnel then revived the wave theory after work on interference and diffraction of polarised light. Young was able to show that light does bend into shadows, if only by very small degrees and he suggested that light was a transverse wave, the medium through which light travelled being disturbed in a direction perpendicular to the direction of propagation. The speed of light was first measured by Fizeau in 1849 and was found to be less in water than air. Newton had predicted the opposite and the corpuscular theory fell from grace. In 1867 Maxwell generated a set of equations which described many properties of electricity and magnetism exactly. He was able to calculate that the speed of propagation of a disturbance in an electromagnetic field was equal to the speed of light and concluded that light was an electromagnetic wave. Subsequently Hertz confirmed this theory by demonstrating that long wavelength non-visible electromagnetic waves could be refracted in exactly the same way as light.

Electromagnetic wave theory however does not explain all the properties of light. In particular there were problems explaining the emission and absorption of light. Classical wave theory predicted that the intensity of radiation emitted should increase with decreasing wavelength, this would result in emission of light of infinite intensity as the wavelength decreased into the ultraviolet. This 'ultraviolet catastrophe' does not occur in practice. Max Plank provided the basis of an explanation. He proposed that energy is imparted into the electromagnetic field in finite quantities or quanta and not in a continuous fashion. Another phenomenon observed by Hertz could not be explained by wave theory. He noticed that a spark was more readily formed between two electrodes when they were illuninated with ultraviolet light. Further study showed that the light prompted release of electrons from the metallic surface of the cathode. This phenomenon is the 'photoelectric effect.' Contrary to expectation of the wave theory this effect persisted even at very low light intensities, there was no threshold below which it could not be observed. Einstein subsequently provided an explanation for the 'photoelectric effect' using Planks ideas. He treated light as being made up of discrete packets of energy or 'photons', the energy of each photon being inversely proportional to the wavelength of the light. Ultraviolet light has a short wavelength with photons of high energy, even at low intensity the energy of each photon imparts enough energy to knock an electron off the surface of a metallic cathode and reduce the voltage required to initiate a spark. It was for this explanation of the 'photoelectric effect' and his application of the quantum theory to light that Einstein was awarded the Nobel prize for Physics in 1921.

The concept of the photon whereby light can take the form of both a particle and a wave, formed the basis of the quantum theory of matter. It had therefore become apparent that both corpuscular and wave theory were required to explain all the properties of light; the propagation of light is best explained using the electromagnetic wave theory.

### 1.4.2 Atomic Structure

Frauenhofer (1797-1826) showed that the wavelength of light emitted or absorbed by a particular element was confined to a number of narrow bands particular to the element. Rutherford (1871-1937) postulated that the atom was comparable to the solar system with electrons orbiting the nucleus as the planets orbit the sun. In 1913 Bohr used the new quantum theory to update the atom model. He argued that electrons should inhabit one of several fixed orbits around the nucleus of the atom.

Electrons in orbit were postulated to contain a 'quanta' of energy which was smallest for orbits of small radius and largest for orbits of large radius. A specific quanta of energy would be required to move the electron from an orbit with a low energy state to an orbit with a high energy state or larger radius. The new theory accurately predicted the wavelengths of the emission spectra of hydrogen.

### 1.4.3 Spontaneous emission of radiation

The quantum of energy required to move an electron to a higher energy state must come from absorbing external energy such as electricity or light and similarly when an electron falls from a high energy level to a lower one there is a spontaneous emission of in the form of a photon of light. The energy of the photon which is spontaneously emitted is equal to the difference between the two energy levels. The wavelength of the light emitted is inversely proportional to its energy and thus light of a certain wavelength is emitted. There may be many potential energy states for a given electron in an atom and thus several given wavelengths may be emitted from a given atom. The emission and absorption of light is best considered using the photon and quantum theory of light.

### 1.4.4 Stimulated emission of radiation.

Einstein predicted in 1917 that emission of a photon from an excited electron within the atom could be stimulated by another photon. The stimulated photon would travel in the same direction as the stimulating photon and would be of equal energy, wavelength, phase and polarity. The stimulating photon would remain unchanged. It was later realised that it may be possible to start a chain reaction whereby the stimulated photon subsequently stimulated emission of other photons from other excited atoms so that the photon flux was amplified. An essential pre-requisite for this process would be the the presence of more excited than ground state orbiting electrons. Unless this applies then photons would simply be absorbed. This situation is called a 'population inversion' and was first achieved by Townes of

Columbia University in 1953. He produced a device which produced electromagnetic waves from the microwave part of the spectrum and was termed a 'MASER' (microwave amplication by stimulated emission of radiation). In 1958 Townes went on to define the prerequisites for construction of the first 'LASER' (Light amplification by stimulated emission of radiation).

### 1.4.5 The optical resonator

Population inversion is difficult to achieve and this explains why the amplification of stimulated emission does not occur easily. It can now be obtained in a variety of substances including solids, liquids and gases in atomic, ionic and molecular forms and is achieved by pumping with energy usually as light or electricity. However in addition to a medium capable of stimulated emission of radiation the other essential component of a laser is an optical resonator. This consists of two mirrors facing each other so that multiple reflections can occur between them. The mirrors are positioned at a distance equivalent to an integral number of half wavelengths apart so that constructive interference occurs. This results in resonance or the production of a standing wave.

### 1.4.6 Maiman's Ruby Laser

The first laser was constructed by Maiman in 1960. The medium was a 1 cm crystal of synthetic ruby on which 2 parallel faces were polished and coated with silver to form 2 mirrors facing each other to form the optical resonator. The chromium ions of ruby were excited using a high power flash lamp to achieve a highly unstable state which quickly decays to a semistable state and it is with this state that the population inversion occurs. When the semistable state returns to ground state emission of a photon occurs at a wavelength of 694 nm. This photon can then stimulate emission of other identical photons and so on. One of the mirrors is only partially silvered so that 5% of the light escapes through it in the form of an intense beam of red laser light in repeated short pulses.

### 1.4.7 Laser light : Monochromatic, Coherent and Collimated

These are the special characteristics of laser light which follow directly from the principals discussed. Many lasing mediums can emit light with a number of discrete wavelengths. Unwanted wavelengths can be blocked by coating the reflective mirrors to block reflection of unwanted bands. Thus laser light can be monochromatic. The beam is also at the same phase at any given point (coherent) and is non-divergent (collimated) and the spot size thus remains fairly constant over large distances.

## 1.5 Optical Fibres

The development of optical fibres capable of transmitting laser light was an essential prerequisite for the use of lasers in gastroenterology. These fibres are elongated glass rods of narrow diameter which are coated. Transmission of light along an optical fibre occurs due to total internal reflection which the coating facilitates. Light travelling along a quartz (glass) fibre which strikes the interface at an angle less than the critical angle is totally internally reflected. Multiple such reflections occur until the light emerges at the far end of the fibre. Laser light is coupled to the fibre by focusing it onto its proximal end. Each photon undergoes different reflections within the fibre and thus the beam is neither coherent nor collimated when it emerges. This has clinical implications as the emerging beam is divergent and thus the power density falls with increasing distance from the tip. Quartz fibres used in gastroenterology can transmit light in the wavelength range 380-1300nm.

## 1.6 Lasers in Gastroenterology

### 1.6.1 The Argon Laser

This was the first laser to find extensive clinical use and the first to be used in gastroenterology. It is a gaseous ion laser which is one of the most inefficient of the lasers. This is because the lasing medium is a gas which normally exists in its atomic state. High currents are required to convert the atoms into ions (by removal of an electron). The argon ions are then excited further to obtain a population inversion. Typically 5 kilowatts input power is required for a laser output of 5 watts. The high power required for these lasers places constraints on the materials required for construction of the discharge tube which is required to withstand high temperatures. Argon lasers do offer outputs at a number of discrete wavelengths as there are several energy levels that excited electrons can fall to. A typical output wavelength for these lasers is 514 or 488 nm. These wavelengths are in the green and blue regions of the visible spectrum and are highly absorbed in vascular tissue and thus protein coagulation can readily be achieved at low powers of a few watts.

### 1.6.2 The neodymium yttrium aluminium garnet (Nd YAG) laser

This is also an ion laser but is not normally described as such as the neodymium (Nd) ions are locked into particular positions by a crystalline host structure. It is thus a 'solid state laser'. The most satisfactory host is the crystal yttrium aluminium garnet (YAG). The laser medium is formed as a rod 10cm in length. Pumping or excitation is achieved by the absorption of incoherent light from a bright incoherent source which is a krypton arc lamp. This lamp is chosen as a larger proportion of its broadband output falls within the narrow band of wavelengths that neodymium ions can absorb. Using such a lamp this laser can achieve an efficiency of 1-2%. This is 10-20 times more efficient than the argon laser. The lamp is also far cheaper to replace than the argon laser discharge tube. The Nd-YAG laser operates in the infrared at 1.06 micrometers. This wavelength is only weakly absorbed in tissue and greater powers are required. An output of 50-100 watts is necessary for endoscopic use and thus the input power of around 5 killowatts is similar to that required for the argon laser.

## 1.7 Laser-tissue interactions

Lasers are sophisticated light sources which can deliver energy with great precision. The delivery of energy to tissue can thus be readily controlled. Within tissue the light can be reflected, transmitted, scattered or absorbed. Biological effects are due to the absorption of light but the other factors determine where the light is disseminated and subsequently absorbed. The absorption characteristics of soft tissues vary enormously between wavelengths giving rise to quite different effects, however studies have shown that the extent of damage depends closely on the energy dissipated (Bown 1980 and 1983). The tissue effects of heat have been discussed in section 1.2. In summary heating initially causes thermal contraction and protein coagulation, as tissue shrinks small vessels are sealed, thrombosis then occurs as a secondary effect. If the volume heated is large vessels up to 1mm in diameter can be sealed (Kelly 1983). If further energy is dissipated carbonization and subsequently vaporisation occurs. At higher Nd YAG laser powers several of these effects can be seen in the same piece of tissue. vaporisation occurs immediately below the beam, deeper there is necrosis with subsequent sloughing and scarring. The extent of different tissue effects can be varied by altering treatment parameters. The Nd YAG wavelength is poorly absorbed by tissue and more of the light is transmitted deeper into the tissue. The Nd YAG laser has a greater power output, and with deeper tissue penetration it is not surprising that superior haemostatic efficiency has been documented in experimental studies than the argon laser (Bown 1980). The bluegreen argon laser light is readily absorbed by vascular tissue and its effects are relatively superficial.

None of the other techniques for coagulation offers the precision of the laser however this may not be necessary for all indications for endoscopic therapy. An important advantage of the Nd YAG laser over other techniques is the ability to vaporise tumour with rapid removal of tumour bulk. Many groups have reported excellent results with this laser (chapter 2).

## 1.8 Therapeutic techniques with Nd YAG laser

### 1.8.1 Oesophageal cancer

Sedation and analgesia are achieved with diazemuls/pethidine. A designated laser endoscope with a large diameter working channel is used, and we find the Olympus 1T 20 (Keymed Ltd, Southend) ideal for this application. It is specially adapted with a safety filter in the eyepiece. We use a 'Flexilase' Nd:YAG laser (Living Technology Glasgow) which can generate up to 100W at a wavelength of 1064nm. It is usually set at 50-70W with a pulse duration of 1 second for treatment of oesophageal cancers. Its output is focused onto the end of a 0.6mm quartz fibre contained in a 2.2mm teflon catheter which stiffens the fibre and allows insertion down the working channel of the endoscope. It also allows a co-axial stream of carbon dioxide or air to be passed which keeps the fibre tip clean and cool and clears the target of blood and debris. The fibre is three metres in length and its distal end is protected by a metal guard. An aiming beam is provided by a low power helium-neon laser which is coupled into the beam path of the Nd YAG. We use a 'non-contact' technique, shaving back exophytic nodules by vaporisation, and treating flat areas by coagulation alone. Insufflated gas and smoke generated by vaporisation is vented by connecting the working channel of the endoscope to an underwater drain using a two way valve which can be closed when endoscopic suction is required. If the procedure lasts more than thirty minutes the scope is removed in order to clean debris from the end, to flush out the suction channel and check patency of the air and water channels. This practice reduces the risk of scope blockage and ensures a better view as the gradual deterioration in vision as smoke and debris adheres to the end of the scope is often not fully appreciated. Necrosed tumour sloughs to a depth of 2-3mm a few days after treatment and patients can undergo further sessions after this period if necessary. Laser treatment is only possible in tumours with exophytic (intraluminal) component; however most tumours come into this category at presentation. Luminal narrowing due to compression by extrinsic tumour is usually dealt with by intubation. Where possible treatment is commenced at the distal tumour margin and proceeds in a retrograde fashion. This avoids the problem of oedema in tissue adjacent to that vaporised limiting forward progress and the lumen is always visualised thus reducing the risk of perforation. Impassable strictures are normally dilated prior to laser treatment so that retrograde tumour destruction can be performed. Occasionally a guide wire cannot be passed and only in these circumstances is laser treatment carried out in a prograde (forward) direction.

### 1.8.2 Rectosigmoid tumours

A sodium phosphate enema is usually adequate preparation for these lesions, more proximal lesions requiring a rectal washout or occasionally a full bowel preparation. Sedation and analgesia are often not necessary but diazemuls and/or pethidine are administered intravenously if required. Access is obtained using a flexible sigmoidoscope or colonoscope with a safety filter in the eyepiece. Air is insufflated and the tumour is washed as necessary to obtain a good view and document the extent of disease as far as possible. The basic instrumentation and technique is exactly as that for treating oesophageal cancers however higher energy treatments are sometimes necessary. Carbon dioxide may be used for insufflation of the bowel as this is partially absorbed and thus reduces the risk of excessive bowel distension. Whenever possible treatment is started at the proximal margin of the stricture and proceeds distally towards the anus as oedema in areas of coagulated tumour can hinder progress forward. Some authors (Brunetaud 1987) advocate an argon laser to treat small lesions up to 4 cm from the anal verge as the Nd YAG laser with its greater power output and tissue penetration can be painful.

### 1.8.3 Difficulties with Non-contact Nd YAG laser for cancers

There are three main problems.

1) Contamination of the fibre tip with blood or debris results in excessive heating of the tip with consequent fibre destruction (fibre 'burn'). In order to minimise this a continuous gas flow is required to keep the tip clean. The flow causes bowel distension which can be uncomfortable.

2) Smoke generated with vaporisation obscures the view until vented, and settles on the endoscope lens in a film, causing a progressive deterioration in visual access and clarity.

3) High power, necessary for tumour vaporisation, can cause a sensation of 'heat' which is distressing to some patients.

Several techniques are employed to minimise these difficulties. Small areas are vaporised at a time allowing heat to dissipate and smoke to vent between shots. If debris is seen on the tip or if the aiming beam is diminished the fibre is removed for cleaning and the scope is removed for cleaning after 30 minutes.

# CHAPTER 2

## REVIEW OF LASER ENDOSCOPY FOR CANCER AND COMPARISON WITH OTHER THERAPIES

### 2.1 Oesophagogastric cancer

#### 2.1.1 Introduction

The incidence of carcinoma of the cardia is rising (Cheng and day 1992). A recent study in Oxfordshire (Rios-Castellanos 1992) found a rate of cardia cancer of 5.2 per 100,000 per year, this had doubled over a 20 year period. This increase is reflected in the overall figures for oesophageal cancer (carcinoma of the cardia and true, squamous cell oesophageal cancer). In 1980 Earlam found a rate of 8 deaths per 100,000 of the UK population per year. More recently the WHO estimates that oesophageal cancer is responsible for about 10 deaths per 100,000 people annually in the United Kingdom (WHO 1988). These tumours most commonly occur in the elderly and present late in their natural history as dysphagia usually does not occur until two-thirds of the oesophageal circumference is involved. Overall at least 60% of all patients are unsuitable for curative treatments (Watson 1988, Desa 1988). The historical long term results for curative surgery and radiotherapy are poor. Earlham's comprehensive review of 1980 found a 5 year survival of 4% and 6% respectively for surgery and radiotherapy for squamous cell cancers. Adenocarcinoma of the cardia has an even poorer prognosis. This review was however historical and retrospective and unrepresentative of the current results in specialist units. There is no doubt that better selection of cases treated in such units gives more satisfactory results. More recent surgical series from the UK indicate an operability rate of 20-40% with a five year survival of 10-15% in those who underwent surgery. (Skinner 1986,Watson 1988, Desa 1988). An up to date study study in gastric cancer (Sue-Ling 1993) shows better results with 53 % of patients undegoing curative resection during 1985-9 and 5 year survival in such patients is probably aroung 70%.

### 2.1.2 Staging oesophageal cancer

Careful staging has demonstrated its crucial importance on prognosis. Eastern surgical series of patients with early lesions have reported five year survival rates of up to 96% (Akiyama 1981, Huang 1981). In the Western world tumours are usually advanced at the time of presentation as screening is not generally undertaken. In large series there are however a significant number of patients with early disease and stratification of patients for stage can reveal surprisingly good results. Watson (1988) noted that five year survival in patients with squamous oesophageal cancer found to be node negative was 50% and this increased to 75% for patients with superficial lesions. Even better results are reported for early stage gastric cancer (Sue-Ling 1993) with up to 90% 5 year survival. Looking at data from several studies Rankin and Mason point out in a recent review on staging (1992) that tumours restricted to the oesophageal wall have a five year survival of 40% compared to 4% for those which have progressed beyond the adventitia. Node negative patients also have a reasonable outlook with five year survival rates of 42% but for those with nodes the figure is 3%. Accurate staging is therefore essential in planning patient management. The finding of a tumour with a low chance of cure does not exclude surgery as primary treatment but at least it is clear from the outset that palliation is the main treatment aim.

Current staging is based on the TNM system. The important criteria for any imaging technique are to determine are.

1) The depth of penetration through the oesophageal wall.

2) Direct tumour invasion into adjacent structures.

3) Involved perioesophageal lymph nodes

4) Distant metastases

CT scanning has been the mainstay of staging until the recent introduction of endoluminal ultrasound which is still only available in a few units in the UK. However CT staging alone of gastro-oesophageal cancer is unsatisfactory (Thompson 1983, Becker 1986). A detailed examination from several studies of CT compared to surgical/pathological staging shows the overall accuracy to be only 39-68% (Rankin 1992). Although CT visualises the intrathoracic oesophagus well, stage 1 and stage 2 (invading muscularis propria) tumours cannot be differentiated and small nodal metastases are frequently missed resulting in understaging.

Endoluminal ultrasound uses a modified endoscope with an ultrasound probe at its tip. The probe frequency is usually 7.5 MHz which gives a depth of field of 5-7cm; lower frequencies will give a deeper field depth but close up definition (of the oesophageal wall) is less detailed (Botet 1991). The instrument is passed through the tumour into stomach and scanning performed as it is withdrawn. Full examination is not possible in all patients (Tio 1990) as the probe will not always pass the stricture. Using this technique excellent oesophageal wall images can be obtained. There are 5 alternating hyper and hypoechoic layers and distortion of the pattern gives the depth of tumour penetration. The characteristics of the nodes are used to define malignant involvement (unlike CT where node size is important). Elliptical, hypoechoic nodes with clearly deliniated margins suggest malignancy. Rankin (1992) reviewed several studies comparing this technique with the resected specimen and found an accuracy of 59-92% for tumour penetration and 69-88% for mediastinal lymph nodes. Diagnosis of infiltration into invading structures is also highly accurate (Tio 1990).

In studies which compare the two techniques (Tio 1990, Botet 1991, Tytgat 1991, Siewert 1990) the endoluminal ultrasound is better for depth of tumour invasion

(92%v 60%) and nodal metastases (88%v74%) but CT scanning better for distant metastases (90%v 70%). In preoperative staging the overall accuracy for both techniques (86%) is better than for each alone. However for monitoring local response to treatment such as radiotherapy or chemotherapy the ultrasound technique should be superior.

CT and endoluminal ultrasound are complex and expensive and may not be necessary. Rankin and Mason (1992) suggest that around 50% of patients can be staged without undertaking such tests. Routine investigations may be enough to stage diseased adequately. Trans-abdominal ultrasound is an excellent technique for identifying liver metastases which can be confirmed by biopsy or cytology if required. Tumours found to be longer than 5cm at endoscopy have extraoesophageal spread in 90% of cases. Laparoscopy may also be useful in staging of cardia cancer (Watt 1989). Some patients have local involvement of neck nodes and a trans cutaneous biopsy may confirm stage 4 disease in such patients.

### 2.1.3 Techniques for palliation

Using the figures quoted above 60% of the 5,000 new cases (3,000 patients) of oesophageal and cardia cancer are suitable for palliation only. Palliative resection restores normal swallowing in 90% of patients who survive the procedure and confers a longer survival than the other palliative procedures available, but carries a high morbidity and a mortality of up to 30% (Watson 1982) although this figure continues to fall with better patient selection and better perioperative care.

Many other treatment modalities are now available for palliation of this difficult condition, including Nd YAG laser therapy, intubation with prosthetic tubes and radiotherapy by external and intracavitary (brachytherapy) methods. Individually there is good evidence for the efficacy of these modalities, but all have their limitations. The important assessment parameters to consider are the quality of swallowing achieved, which is a key factor in overall quality of life (Barr 1990a, Loizou 1991), and the price paid to achieve that quality (procedure related complications, time in hospital for procedures, number of procedures).

Most of the studies of palliative treatment for oesophageal cancer have been uncontrolled, and some have studied small numbers of patients. Many only examine one treatment modality but even when treatments have been compared patients have often not been randomised and historical controls are frequently used. This makes interpretation of results difficult. This review concentrates on the larger more recent studies and those which have compared the important treatment modalities.

### 2.1.3.1 Intubation

Surgical intubation procedures carry a high morbidity and mortality (Watson 1982, Urschel 1991) and have been largely replaced by endoscopic methods which are safer and equally effective (Ogilvie 1982). Despite this improvement there is a risk of procedure related perforation of 5-10% (Ogilvie 1982, Gasparri 1987, Tytgat 1986, Barr 1990, Loizou 1991a). Mortality rates are usually less than 10% but figures as high as 31% have been reported (Diamantes 1983). Such a high rate to some extent reflects the grave condition of many of these patients; however rates this high have not been recorded with other palliative treatments. Potentially serious long term complications are reported in all series and can occur in anywhere up to 50% of patients. They include tube displacement, blockage, overgrowth and late perforation. These rather disappointing figures for morbidity and mortality with endoscopic intubation have generated interest in endoscopic laser therapy. The other important reason for such interest is that tubes do not fully restore swallowing, most patients will only manage a semi-solid diet and some will not manage more than fluids.

### 2.1.3.2 Nd YAG Laser

The use of the Nd YAG laser for recanalisation of oesophageal cancers was first reported in 1982 and further details published in 1983 (Fleischer). Other groups confirmed that this treatment was effective and safe (Krasner 1987, Bown 1987), and there is now considerable worldwide experience. A multicentre inquiry (Ell 1987) on 1359 patients showed initial success in 83% of patients and a serious complication rate of 4% of which around half were perforations. An early study from our unit (Bown 1987) was representative of the general experience. Around three-quarters of 34 patients treated were able to manage at least some solid foods after a course of treatment although most of those who survived more than a short period needed to return for regular repeat treatments every 5 weeks or so. This has led some authors to recommend regular repeat treatments regardless of symptoms (Krasner 1987, Barr 1990).

Others have tried to identify groups of patients who are more likely to do well with laser. Fleischer (1985) suggested that patients with short lesions (<5cm) in a straight segment of the mid and distal oesophagus were likely to do best. He found that those with cervical tumours did not respond well with laser. We have achieved better results with laser in these patients but when laser fails the problem can be successfully addressed with a modified oesophageal prosthesis (Loizou 1992). Fleischer also suggested that patients with soft non-constricting circumferential tumours which would not hold a prosthesis well were good candidates for laser. In contrast obstruction secondary to extrinsic compression or infiltrating tumour and long stenotic lesions were felt to be best treated with intubation. Naveau (1990) expanded on this theme. Patients with adenocarcinomas, an initial length < 6 cm and those who improved after initial laser treatment were all independently correlated with longer 'symptom improvement duration'. The authors concluded that patients with squamous cell cancers longer than 6 cm should be entered into trials of other palliative techniques. In a larger more recent series (Mason 1991), with 189 patients, it was not possible to identify prognostic factors at initial endoscopy and the authors policy was to initially treat all patients with laser subsequently intubating those who do badly. A subsequent study from the same unit showed that survival was better in patients with less severe dysphagia at presentation (Derodra 1992). Our own policy is similar to that of that of Mason. If there is polypoid tumour treatable with laser we try this approach first unless the prognosis of the patient is felt to be very poor (Loizou 1991).

In summary laser treatment for cancer of the oesophagus and gastric cardia offers rapid relief of dysphagia, can be performed as an out patient procedure if the patients general condition allows, does not have systemic effects and serious complications occur in less than 5% of patients. The major drawback is the need for regular repeat treatments every 5 weeks or so to maintain adequate swallowing

#### 2.1.3.3 Bipolar electrocoagulation

Johnson first reported use of the BICAP probe (3 pairs of bipolar electrodes) for recanalisation of oesophageal tumours in 1987. A special tumour probe was used which is inserted into the oesophagus separately from the endoscope. Only 20 patients were treated and 4 of these developed serious complications including late bleeding and fistula formation. Further evaluation of this probe was performed by Jenson in 1988. Fourteen patients were treated with laser and 14 with BICAP and results compared. Both modalities were effective at relieving dysphagia (86% patients improved). One patient in the BICAP group developed a fistula but no serious complications were seen with laser. The authors concluded that BICAP was equally good for circumferential tumours but that laser was safer for exophytic non-circumferential tumours because it could be directed endoscopically. A small study on 30 patients comparing BICAP with oesophageal prosthesis (McIntyre 1989) demonstrated no benefit in terms of swallowing for the probe. Complication rates were similar, there were 2 perforations during dilatation (one in each group), one patient perforated on tube insertion and one patient developed an tracheooesophageal stricture after probe treatment. Patients treated with the probe needed repeat sessions every 28 days. These studies are rather small to make a final judgement but the relatively high rate of serious complications encountered with this tumour probe is worrying.

### 2.1.3.4 Alcohol injection

Encouraging results have been reported for injection sclerotherapy with absolute alcohol (Payne James 1990). Alcohol causes tissue death by desiccation. The treated area subsequently sloughs to leave a recanalised lumen. The relief of dysphagia was similar to that achieved with the Nd YAG laser and the technique appeared safe. The ability to vaporise polypoid tumour with laser cannot however be achieved and it is likely that dysphagia is not relieved as rapidly in many patients. Studies on alcohol injection into liver deposits undertaken at UCH demonstrate the difficulty in controlling the distribution of injected alcohol. The extent of tissue damage is accordingly difficult to predict and extensive damage may conceivable increase the risk of complications such as delayed fistula formation or perforation.

### 2.1.3.5 Comparative studies of laser and tube

At the time of writing there have been 8 studies directly comparing laser and tube. These are documented in table 2.1 Four (Carter 1986, Buset 1987, Hahl 1991, Loizou 1991a) were not randomised and the other 4 were (Barr 1990, Alderson 1990, Fuchs 1991, Carter 1992). Only six of the studies looked carefully at dysphagia control (these studies looked at 253 patients in total) 4 showed laser to be superior and 2 showed no difference. Most studies agree that the morbidity rates with laser are substantially lower than with tube. The exact figures are given in the table. The mortality associated with tube insertion is up to 11% (Hahl) and in the largest series is 4.3% (Buset). This is in marked comparison to the occasional patient who dies with laser treatment (2 patients in these series ; one in Aldersons and one in Carter 1992).

**Table 2.1 Details of all 'head to head' comparisons of Nd YAG laser and tube**

| | Patient number | Best dysphagia relief | Laser complications | Tube complicatons |
|---|---|---|---|---|
| ***Randomised studies*** | | | | |
| Alderson 1990 | 40 | laser | 4 (20%)<br>3 perforations<br>1 bleed | 4(20%)<br>1 perforation<br>2 displacements<br>1 overgrowth |
| Barr 1990 | 40 | equal | 2(10%)<br>2 perforations | 12(60%)<br>4 bolus obstr<br>3 perforations<br>4 overgrowths<br>2 displacements<br>1 bleed |
| Fuchs 1991 | 40 | equal | 1(4%)<br>perforation | 8(47%)<br>1perforation<br>4 displacements<br>1 overgrowth<br>2 bolus obstr |
| Carter 1992 | 40 | laser | 5 (25%)<br>3 perforations<br>1 pneumonia<br>1 fistula | 9 (45%)<br>3 bolus obst<br>1 overgrowth<br>4 pneumonia<br>1 failed |
| ***Non randomised studies*** | | | | |
| Carter1986 | 10 tube<br>10 laser | laser | 4 (40%)<br>1 fistula<br>3 perforations | 5 (50%)<br>3 overgrowths<br>2 displacements |
| Buset 1987 | 116 tube (14mm)<br>28 laser | equal | 1 (4%)<br>1 perforation | 47 (40%)<br>9 perforations<br>4 haemorrhage<br>3 pneumonias<br>21 displacements<br>4 bolus obstr<br>3 overgrowth<br>2 oesophagitis<br>1 pressure necrosis |
| Loizou 1991 | 30 tube<br>43 laser | laser | 1 (2%)<br>1 perforation | 11 (37%)<br>4 perforations<br>7 bolus obstr/<br>displacements |
| Hahl 1991 | 27 tube<br>69 laser | equal | 6(9%)<br>4 perforation<br>2 sepsis | 13 (48%)<br>2 pefroration<br>2 massive bleed<br>6 bolus obstr/<br>displacements<br>3 misc |

The study from our own unit comparing laser with intubation (Loizou 1991a) has given us a better insight into which patients are likely to benefit most, in terms of quality of swallowing, from each of these modalities. Solids can be managed for more than half the survival time in 1 in 3 of those treated with laser but only 1 in 10 of those intubated. In addition the proportion of patients managing fluids only is double in patients intubated compared with patients receiving laser therapy (19% v 8%). In simple terms around 1/3 of these patients will swallow better with laser than a tube for more than half the time. The results for tube indicate that more than 70% of those intubated will manage at least semi-solids. Overall the group receiving laser required more procedures (mean 4.6 v 1.4) but the risk of perforation was high (13%).

Laser therapy is thus demonstrated capable of providing more effective and safer palliation than tube. The tube, however is a useful secondary therapy for patients who do do not respond to laser or who are late laser failures. In our unit it is now standard policy to treat patients with inoperable tumours with laser as first line treatment. Patients who are anorectic and in poor general condition who would not undergo repeated endoscopic laser treatments easily are also advised to have a tube as first line treatment.

#### 2.1.3.6 External Beam Radiotherapy

External beam radiotherapy has been used extensively for many years in the treatment of squamous cell carcinoma of the oesophagus. Most patients treated have been considered unsuitable for surgery. Historically it has been used aggressively with cure as the main aim. The hope was that such treatment would lead to prolonged remission of the tumour and symptoms even if cure was not actually achieved. An extensive review of radiotherapy for oesophageal cancer (Earlam 1980) however, revealed a one year survival of only 18% and a five year survival of 6%, though selected cases do better. The results for radical surgery were similar. Subsequently Earlam (1991) attempted to perform a multicentre randomised study of radiotherapy and surgery for squamous cell cancer of the oesophagus but unfortunately there was insufficient support from surgeons. His results for radiotherapy (Earlam 1990) in patients with operable and inoperable squamous cell cancer of the oesophagus were impressive. One year survival in these groups was 46% an 16% and 5 year survival 14% and 4% respectively.

There is still some argument over the treatment of choice for patients with squamous cell oesophageal cancer who are operable. Some would argue that radiotherapy is as effective as surgery, others take the opposite view (Cuschieri, Earlam, Khoury 1991).

A recent study from the Christie Hospital, Manchester, demonstrated a five year survival of 16% in patients with cancer of the upper third of the oesophagus (Slevin and Stout 1989). However earlier series have found up to 20% of patients initially enroled for curative treatment are unable to tolerate a radical course of radiotherapy (Wara et al 1976).

In the last 10 years the importance of palliation of symptoms has been acknowledged and subsequent studies (of all modalities) have often considered relief of dysphagia as well as survival times. Despite this change in emphasis there have been relatively few publications looking at palliation of dysphagia with radiotherapy alone. One early study did, however, note that external beam radiotherapy usually relieves dysphagia slowly, often taking several weeks for maximal effect and only half the patients respond (Pearson 1978).

Two studies (Mellow 1984, Karlin 1987) prospectively compared laser treated patients with historical controls treated with external beam radiotherapy. Both studies were small and both focussed on survival which was longer in laser treated patients.

Caspers et al (1988) performed a retrospective but detailed analysis in a large cohort of patients with inoperable oesophageal cancer palliated with external beam radiotherapy. The mean age was 64.5 years (range 36-92). They found an improvement in dysphagia in 70% of 127 patients, and 50% remained palliated to death. Survival was longer in patients treated with higher radiotherapy doses (more than 50 Gy in 5 weeks). Patients who could not swallow semi-solids before treatment started survived for a shorter period, (6.4 versus 8.7 months), although some patients whose swallowing was initially poor did improve with treatment. It is of particular interest that patients with adenocarcinoma did as well as those with squamous cell tumours. A second study (Cederqvist et al 1978) also found no difference in survival or radiosensitivity of the two tumours.

Earlam (1990) also reports relief of dysphagia in a group of 11 patients with non resectable adenocarcinoma of the stomach and oesophagus treated with palliative radiotherapy (mainly 40 Gy).

#### 2.1.3.7 Brachytherapy

Intracavitary irradiation (brachytherapy) has been available for many years but has attracted attention recently, as it can be applied by remote controlled afterloading units such as the 'Selectron' (Rowland 1985). This makes the procedure quick and simple, and staff are not exposed to radiation. Using this technique a relatively high dose of radiotherapy can be applied circumferentially to the tumour from within the oesophagus via a nasogastric tube. As the treatment dose falls off rapidly from the source, the volume of normal tissue exposed to the irradiated field is less than with conventional radiotherapy thus limiting systemic side effects. Unfortunately this also means that regional nodes cannot be treated as effectively as with external beam radiotherapy. Results to date have been encouraging, although oesophagitis can be troublesome and clinical experience is limited. Rowland treated 40 patients with a single 15Gy fraction. Relief of dysphagia was achieved for a median of 12 weeks for adenocarcinomas and 15 weeks for squamous cell cancers. Two patients were successfully retreated after 30 weeks. Only 5 patients suffered with oesophagitis and there was no mortality. In a randomised study (Low 1992) 23 consecutive patients received laser or brachytherapy. Initial improvement in dysphagia was slightly better with laser (91% v 83%) and was well maintained at 2 months in both groups (81% laser, 75% brachytherapy). Retreatments were three times as common with laser but dysphagia was relieved more rapidly. Most complications were minor with both treatments although there was one perforation with laser. Other complications with brachytherapy which probably occur more commonly if patients also receive external beam treatment include oesophageal ulceration, fistula and stricture (Hishikawa 1984).

### 2.1.3.8 Radiotherapy combination treatments

One recent retrospective study (Oliver 1990) looked at the combination of radiotherapy with endoscopic intubation in inoperable squamous cell oesophageal cancer. Twenty one patients treated with intubation alone were compared with the same number treated by intubation plus external beam radiotherapy. Those receiving radiotherapy were selected cases thought to be 'fit' for such treatment and thus would be expected to do better. Patients who died within 30 days of the start of treatment were excluded. Clearly this study could not use dysphagia as an end point, and survival was analysed. The study was not randomised and although those who received radiotherapy survived longer (median 188 days versus 98 days) the difference was not statistically significant. The authors concluded that a controlled trial of radiotherapy in these patients is needed.

A promising early report (Bader 1986), looked at laser followed by brachytherapy for oesophageal malignancies. The attraction of this approach is that good swallowing is established rapidly with laser and there is the possibility of allowing deeper penetration of brachytherapy treatment by removing luminal tumour first with laser. Those with adenocarcinomas received 7 Gy at 1 cm distance up to 6 times and those with squamous cell cancers the same regime up to 2 times but they also received external beam radiotherapy. Only 11/48 patients developed recurrent dysphagia with a mean survival of 5.9 months in 16 patients who had died. No further details are given.

More recent studies have looked at the combination of laser followed by brachytherapy and the results appear promising. Sander (1991) performed a prospective randomised comparison of laser with laser followed by brachytherapy in 39 patients. A modest radiotherapy dosage was applied (7 Gy at 1 cm from the source) on 3 occasions at weekly intervals for each patient. Mild oesophagitis was only seen in 4 of 19 patients receiving radiotherapy. The dysphagia free interval was prolonged from 30 to 65 days in those with squamous cell cancers treated with brachytherapy but there appeared to be an increase in the number of procedures required for patients with adenocarcinomas. Three patients in each group developed fistulae and were intubated.

Renwick (1992) treated twenty one patients with laser and a single brachytherapy treatment at a dose of 15 Gy one cm from the source. The improvement in swallowing was impressive, with all patients except 2 (who had disseminated disease and died early) managing a solid or semisolid diet. Adenocarcinomas appeared to respond as well as squamous cell tumours. Only five patients required further therapeutic endoscopy although it is not clear how follow up was performed.

Combining brachytherapy with external beam treatment is another promising approach (Agrawal 1992). In this study 67 patients were treated; most received 10Gy at 1 cm by brachytherapy and the external beam dosage varied from 20-50Gy. Just over half required dilatation for recurrent dysphagia. Two patients developed severe oesophagitis and there were 4 fistulae. One year survival was impressive at 42%.

### 2.1.4 Comments

Comparing results between studies is difficult because of problems with patient selection. Those referred to radiotherapists are clearly a different group, they are more likely to have squamous cell cancers and are probably in better general condition than patients referred for laser or tube. Many studies have selected fitter patients for radiotherapy treatment (Oliver 1990) and this may explain why they do better. It is thus only by performing randomised comparisons of treatments that true differences can be detected.

## 2.2 Rectosigmoid Cancer

### 2.2.1 Why minimally invasive treatment?

It is generally accepted that the ideal treatment for colorectal cancer is surgical resection. Unfortunately at least 10% of patients have tumours too extensive to resect or are unfit for open surgery. Early surgical studies looked in detail at survival rates and did not examine morbidity. Gill (1978) reported a hospital mortality of 5.5% for resection of colorectal cancer but morbidity is not discussed. Hughs (1980) recorded an overall mortality of 6.7% (94 patients) for resection of the rectum in a series of 1395 patients over a 25 year period, however in patients over the age of 70 years the mortality was 15%. Again morbidity was not discussed. Results from specialist centres can be more impressive. One series (Goligher 1984) found 93% of patients to be operable. Seventy nine percent of resections were performed with a chance of cure and the operative mortality in this group was only 2.8%. More recently in a large multicentre trial (Phillips1985) involving 94 surgeons and nearly 5,000 patients there was an operative mortality of nearly 10% for curative resection in non-obstructed patients. Including obstructed patients this rose to 23%. Potentially serious complications (Intra abdominal sepsis with or without leaks or cardiopulmonary complications) occurred in almost 30% of patients and wound infection/haematoma in a further 20%. The figures for palliative resection are even less satisfactory. Many studies do not present this data separately but Goligher reports a mortality of 21% for such procedures.

Many of these studies include patients treated two and three decades ago and it could be argued that better surgical techniques and post operative care and the widespread use of prophylactic antibiotics should improve results. Unfortunately these developments have been at least partially overshadowed by an increasing proportion of elderly patients. Several authors have looked at perioperative mortality in the elderly associated with resection of colorectal malignancies. Mortality rates of 18% and 36% have been reported in older studies (Cohen 1978, Jensen 1973). More recent studies found a mortality of only 8% (Wobbes 1985), and 10% (Bader 1986) in the elderly group. However morbidity was 33% in the latter study for patients over 75 years.

A detailed study from the Royal Free Hospital (Lewis 1988) studied 277 consecutive patients with colorectal cancer aged over 70 years. The overall mortality was 11%. However after palliative resection of tumours with local spread the mortality was 9/44 (21%) and with distant spread 12/32 (38%). After curative resection the mortality was only 2% in the under 70 age group and 7% in the over 70's. The authors conclude that age alone should not be taken as a contraindication to surgery although the risk of death from major complications after palliative resection in particular should be taken into account.

It is also important to consider the prognosis of patients surviving palliative resection. Hohenberger (1986) found a median survival of only 8 and 14-16 months in patients undergoing palliative resections with and without liver metastases. A second group, Moran (1987) found a survival of 6 months in those treated only by diverting colostomy and 15 months in those resected. Those treated with a proximal diverting colostomy only benefit from relief of obstructive symptoms and troublesome bleeding/discharge usually continues. The limited survival in such patients raises the question whether open surgery with its attendant risks and period of hospitalisation is warranted. Clearly there is a group of patients who would benefit from a less aggressive local palliative treatment. A recent review on advanced rectal cancer (Alexander-Williams 1990) takes up this theme and advises that surgeons should select those patients for whom radical excision will not be curative and treat with local methods which are cost effective and carry a low morbidity and mortality.

Elderly patients with advanced rectal disease are clearly likely to benefit from a minimally invasive approach. Patients with distant metastases and those with concurrent medical disease which makes surgery risky are also candidates for such an approach.. Rectal lesions are well suited as they are easily accessible to local treatment, the safety margins below the peritoneal reflexion are greater and resection in this region technically more difficult.

In the UK the incidence of colorectal cancer is around 30,000 per year (Kings Fund Forum 1990). Assuming 10% are unsuitable for surgery there are around 3,000 patients a year who require palliative treatment.

### 2.2.2 Clinical experience

#### 2.2.2.1 Nd YAG -laser

Endoscopic laser tumour photoablation was introduced in 1981 for treatment of rectosigmoid cancers. Describing initial observations at UCH, Bown (1986) carefully documented the outcome in 17 patients with rectosigmoid cancers who were considered inoperable due to advanced age, liver metastases or severe concomitant disease and were treated with Nd YAG laser. Pretreatment symptoms included rectal bleeding, diarrhoea, mucous discharge, tenesmus, abdominal pain and constipation due to obstruction. Treatment produced a significant improvement in 15 patients (88%). One of the patients in whom treatment failed developed obstruction and required a diverting colostomy, though the improvement in symptoms was marked, and along with details of symptoms relieved in other studies these are shown in table 1. Bleeding diminished in 11 of 12 patients, diarrhoea improved in all those with increased bowel frequency and faecal incontinence was controlled in 4 of 5 patients. Obstructive symptoms were improved in 7 of 8 patients and at least some relief in tenesmus occurred in the same number. Eleven (65%) were fit enough to go home between treatments, requiring an average of 2.5 treatments (range 1-6) with an average hospital stay of one week. Three patients suffered recurrent symptoms severe enough to require further laser treatment, but the survival of the group as a whole was short, explaining why so few required treatment after the initial course and reflecting the advanced stage of disease of the majority. Fourteen patients died 1-39 (mean 15) weeks after treatment though three patients with small lesions were still alive 39-54 weeks after treatment. Most passed small amounts of blood or mucus and a few complained of rectal discomfort after treatment. There were, however, no cases of perforation or delayed haemorrhage. Several subsequent studies published in quick succession (Escourrou 1986, Naveau 1986, Mathus-Vliegen 1986a and 1986b, Brunetard 1987) confirmed effective symptomatic palliation in several hundred patients with advanced rectal cancer. These studies document palliation of rectal bleeding in 71-92 % and obstruction in 47-87 %. The mean number of sessions required per patient is 3 or 4 in most series, although any number up to 40 sessions have been reported. Most patients are discharged after short periods of hospitalisation. The serious complication rate in some of these series was as high as 11% although the frequency in our own unit is 4%. The main complications have been perforation, haemorrhage, fistulae/abscess and stenosis, the latter two more likely from progressive tumour growth in most patients, rather than laser fibrosis. In all series the laser related mortality is low (around 1%). Details of symptomatic palliation and serious complications in the larger and some of recent studies are given in table 2.2.

Table 2.2 Symptoms relieved and serious complications with Nd YAG laser treatment for rectal cancers

| | No. patients | Bleeding/discharge | Obstructive symptoms | Overall | Serious complications |
|---|---|---|---|---|---|
| Mathus-Vliegen* (1985) | 84 | 37/40 (92%) (Bleeding) | 20/24 (83%) | 76†/84 (90%) † included 20 patients with bleeding and obstruction | 11/84 (13%) 6 Perforations 3 Stenosis 2 Bleeding |
| Bown *et al.* (1986) | 17 | 11/12 (92%) (Bleeding) | 7/8 (87%) | 88% | 1/17 (6%) Stenosis |
| Brunetard *et al.* (1987) | 85 | 88% (Rectal discharge) | 7/15 (47%) | 72/85 (85%) | 2 (2%) 1 Perforation 1 Abscess |
| Loizou *et al.* (1990) | 42 | 23/27 (85%) Initial 78% Long term (rectal discharge) | 11/15 (73%) Initial 67% Long term | 34/42 (81%) Initial 31/42 (74%) Long term | 2 (5%) Perforations |
| Chia *et al.* (1991) | 27 | 17/17 (100%) (Bleeding) | 10/10 (100%) | 27/27 (100%) | 0 |
| Daneker *et al.* (1991) | 37 | | 84% | 84% | 3/37 (8%) 1 Perforation 1 Bleed 1 Myocardial infarction |
| Dittrich *et al.* (1992) | 27 | | 6/6 (100%) | | 3/27 (11%) 1 Perforation 1 Fistula 1 Pulmonary embolism |
| Bright *et al.* (1992) | 38 | | Poor (figure not stated) | 8/32 (25%) | |

* A Retrospective multicentre analysis (published in 1986) looking at the same parameters in 181 patients produced similar results.

The best documented of these series is from Brunetaud (1987), who treated 95 patients with rectosigmoid cancer. Ten had exophytic tumours < 3cm in diameter (group 1). Eighty five had advanced disease and were a similar group to those discussed above (group 2). Seven patients were treated with argon in addition to Nd-YAG laser for tumours close to the anal verge. The criteria used for treatment assessment in group 2 were a subjective improvement and relief of symptoms as follows; disappearance of mucous discharge, ease of stool emission, reduction to less than two bowel movements per day with no nocturnal stools or constipation, and no more than 2 bloody stools per week.- strict criteria by any standards.

Seventy two patients (85%) in this group improved, with an average of 2.5 treatments over 2 weeks. These patients were carefully followed to death and although survival decreased rapidly with time (61%, 38%,and 19% at 6,12, and 24 months respectively) the proportion well palliated remained fairly static until 12 months before falling slightly to 68% at 24 months. Few of these patients had obstructive symptoms but the number successfully palliated was low (7/15, 47%) in comparison with other studies.

Using circumferential involvement as the criterion the authors further divided patients with advanced tumours into three categories: C1 < 1/3, C2 > 1/3 and < 2/3, and C3 > 2/3. This categorisation proved very useful as a predictor of symptomatic relief. There were no treatment failures in 11 patients treated in the C1 group, just one failure in 38 patients in the C2 group and 12/36 failures in the C3 group.

Group 1 patients (tumours < 3 cm diameter) all presented with minimal bleeding without evidence of ulceration or submucosal infiltration of the bowel wall. They were unsuitable for surgery due to age or concomitant medical conditions. Surprisingly complete destruction with a biopsy negative scar was obtained in all 10 patients. An average of 4 laser treatments were given over 5 months. No local recurrences were seen but one patient died of peritoneal metastases after 8 months. Two patients died at 18 and 25 months from pre-existent non-malignant medical problems and 2 were lost to follow up. Five patients remained well with a mean follow up of 18 months. There were only 2/95 serious complications in the whole series (2%); one patient suffered a fatal perforation and another developed a perirectal abscess which resolved with medical treatment.

Loizou (1990) studied 49 patients with rectosigmoid cancers unsuitable for surgery due to advanced disease, high surgical risk or refusal of surgery. He pointed out the difficulty in assessing symptoms in an objective manner and therefore defined treatment success as the ability of the patient to lead a lifestyle appropriate for his or her age and general condition, without constant concern for bowel function. Seven had small tumours < 3 cm in diameter corresponding exactly with Brunetaud's group 1 patients. The remaining 42 had advanced tumours, 34 with > 2/3 circumferential involvement. About 60% of these patients would have required a permanent colostomy if managed surgically. Eighty-one percent showed initial improvement and in 74% this was maintained in the longer term. Prolonged palliation of obstructive symptoms (67%) was seen less often than palliation of rectal discharge and tenesmus (78%).

Treatment failures occurred only in patients with extensive tumours (8 initial, 3 late). In order to identify prognostic indicators, patient and tumour characteristics were examined. A greater proportion of patients (100%/76%) were palliated initially in the group with C2 tumours than C3 tumours. However neither the indication for laser treatment, symptomatic presentation, tumour location nor tumour length appeared to have any prognostic significance.

Four patients with symptomatic early tumours all enjoyed relief of rectal discharge and/or tenesmus. All died of unrelated disease (13 to 20 months) although complete tumour eradication was achieved only in one. Complete eradication was also achieved in 3 other patients with early tumours all of whom were asymptomatic (follow up 12 to 28 months) though one also received a course of radical radiotherapy (60Gy). Perforations occurred in 2 patients with impassable lesions at the rectosigmoid junction but no patients died as a result of treatment.

McGowen 1989 examined quality of life in patients treated with laser for inoperable rectal cancer. Fourteen patients were studied before and after treatment, using a standard quality of life index and a linear analogue self-assessment. Where local symptoms were prominent and well controlled, the quality of life scores improved, though patients suffering from pain and the general effects of malignant disease showed no improvement. These results support the general findings from earlier studies of all palliative modalities.

Some authors (Kiefhaber 1986, Dittrich 1992) have successfully used the Nd YAG laser for preresectional recanalisation for obstructing colorectal malignancies. Although the total number of patients so treated is small (54 and 29 patients respectively in these series) most of these patients were adequately recanalised so that one-stage resections were possible and diverting colostomy was avoided. In the larger series total in-patient mortality was 9%, this was considered to be a marked improvement of a mortality of 24-40% for staged operations.

In contrast to the studies discussed so far two groups (Van Custem 1989, Bright 1992) report less satisfactory results with advanced tumours. The first study reports only 51% of patients were initially palliated; this fell to 25% of surviving patients at 18 months. The second reported failure of treatment in 18/26 patients with advanced disease although those with small tumours did well.

The poor long term results in the first study were attributed to progressive growth of the extrinsic component of the tumour, beyond the reach of safe laser treatment. One explanation for this may well be that patients were re-treated only when they developed further symptoms, and not electively as in most studies. This resulted in long treatment intervals (average 4.7 months) which in our experience leads to growth of massive tumours which are difficult to control endoscopically. In the second study many patients became incontinent, probably partly due to a high proportion of patients with low tumours invading the sphincter, although the authors suggest that fibrosis (with loss of rectal compliance) may be responsible. This group also reported poor results in those presenting with obstruction.

These poor results reinforce the fact that the Nd YAG laser alone is not ideal for all patients with advanced disease and that long term results may be more operator dependent than would be ideal.

#### 2.2.2.2 Comparison of Nd YAG Laser with surgery

Despite the extensive experience with the Nd YAG laser for advanced rectal and rectosigmoid cancer there have been few formal comparisons with palliative surgery. Ideally a prospective randomised study should be performed but there are very real difficulties in setting up such a study. A recent study from the authors unit attempted a comparison of laser treatment and surgery in patients with advanced disease (Loizou 1989). The laser group were those patients with advanced tumours in the study previously discussed and the surgical group were historical controls. The two groups were well matched in terms of sex ratio and symptomatic presentation although the laser group were older, had a higher proportion of low rectal tumours (55%/34%) and advanced rectal disease (55%/19%). Thus there was a negative bias against laser therapy. Overall symptomatic palliation was similar in the two groups, laser 74%, surgery 85%, but surgery proved superior in palliating obstructive symptoms. Palliative surgery however carried a mortality of 8.5% against 0% for the laser group, the morbidity of surgery was also greater and cumulative hospitalisation time was 4.5 times greater in the surgical group.

Survival was longer in the surgical group (mean 7.7/4.6 months). Sub group analysis showed that patients with liver metastases undergoing complete resection of local disease were living longer than patients with liver metastases treated with laser. This may have been due to patient selection because those treated with laser probably had a greater tumour load. There was however no difference in survival between the two treatments in patients with advanced locoregional disease. (In this group the tumour could not be completely resected in patients undergoing surgery).

A similar study comparing the two approaches (Mellow 1989) found a longer survival in patients with metastases treated with laser (36 weeks against 28 weeks). This study also found the complications (19/35 and 3/21), length of hospital stay and cost ($23,000/12,000 in patients with metastases) to be significantly greater in patients undergoing surgery.

The only significant disagreement between the results of these studies is the survival in patients with liver metastases. The acknowledged bias against the laser treated group in the first study may account for these differences. However as neither of these studies were randomised comparison of survival data is likely to be unreliable. In any case survival duration in these patients is not the most important aim of treatment.

### 2.2.2.3 <u>External Beam Radiotherapy for rectosigmoid cancer</u>

External beam radiotherapy is commonly used as adjuvant post-operative treatment for Dukes B and C rectal cancers. It can also be employed pre-operatively and may be of particular use in treating inoperable cancers in the hope of reducing tumour bulk sufficiently to allow resection. However it also used, increasingly, as the sole therapy for rectal cancer, typically for advanced inoperable cases.

The first detailed series was reported by Williams in 1956. One hundred and eighty nine patients presenting between 1937 and 1954 were treated with supervoltage radiation. Eighty two percent were inoperable, most of the remainder were judged unfit for a surgical procedure due to age or infirmity. The average age was 60 years. The treatment regime was aggressive, a dose of 60 Gy to the tumour volume over 6 to 8 weeks being attempted though not always achieved. Complete relief of symptoms was reported in 76% of those with rectal bleeding, 55% with tenesmus, 48% with pain and 47% with mucous discharge. Many more patients benefited with partial symptom relief and these figures are given in table 2.3). Patients presenting with obstructive symptoms required colostomy before radiotherapy; taken together with those later requiring colostomy for radiation fibrosis, this came to a total of 103 patients (55%).

Fifty per-cent of patients had the treatment regimen interrupted or modified because of radiation reaction, usually bladder and bowel toxicity and occurring after the second week of treatment. All settled without serious hazard. Serious or potentially serious late complications affected 28% of patients in all. Twelve (6%) developed fistulae (mainly rectovaginal) and 'chronic radiation necrosis' occurred in 9. Thirty two patients (17%) developed fibrosis leading to rectal stenosis, and although many patients already had a colostomy,others then required one for relief of obstruction.

Overall 33% survived 2 years, 14% 3 years and 5% 5 years. Survival was better in patients with early disease. The authors concluded that cure of advanced disease could occasionally be obtained in patients without metastases at the time of presentation.

The incidence of radiation-associated complications in this study was high, probably due to the doses used. Modern megavoltage equipment and lower dose regimen have reduced the incidence of complications in more recent series.

Later studies have mostly supported these findings. Several authors have used lower dose regimen (Wang 1962, Soleimani 1972, Rao 1978, Stearns 1975) which reduces the incidence of complications. The response and duration of palliation however are related to the radiation dose. A useful traditional approach was to treat initially with 20 Gy over 2 weeks and repeat if necessary. Long term palliation was often not addressed in detail though the implication was that symptomatic relief was maintained. Wang however noted that of 69 patients initially palliated with 21-30Gy at 10Gy per week, only 12% had benefit lasting more than 6 months while 58% of those receiving 41-50 Gy had response after 7 months. Many studies do not discuss treatment complications although, as expected, they appear be less common with lower dose treatment. James (1983) records 21/111 patients suffering with bowel disturbance after palliative radiotherapy doses with only 8 judged to be severe. No other complications were noted.

There have been few recent studies since the widespread introduction of megavoltage radiotherapy. One (Allum 1987), reported similar results in patients treated with single dose fractions of 10 Gy to others using a fractionated course to 45 Gy (Megavoltage radiotherapy). Two thirds of patients in each group were relieved of pain for a period of 3 months. A second recent study using megavoltage radiotherapy also demonstrated good palliation (Taylor 1987). Seventy four patients with recurrent or inoperable rectal cancer were treated to 30-35 Gy in 10-15 fractions. Overall 77% of them benefited from improvement in symptoms. Complications were generally minor, 31% suffering with diarrhoea or tenesmus following treatment; serious complications were not seen. A summary of symptoms relieved and serious complications for 4 important studies is given in table 2.3.

Table 2.3 Symptoms of advanced rectal cancer relieved with external beam radiotherapy

| | No. patients | Bleeding | Mucous | Tenesmus | Pain | Serious complications |
|---|---|---|---|---|---|---|
| Williams *et al.* (1956) | 189 | 121/135 (90%) | 77/116 (66%) | 48/66 (73%) | 78/102 (76%) | 50 (26%) 12 (6%) Fistulae, 6 (5%) chronic radiation necrosis, 32 (17%) (rectal fibrosis) |
| Wang and Schulz (1962) | 111 | 19/20 (95%) | | | 63/78 (81%) | Not discussed |
| Taylor *et al.* (1987) | 145 | 39/46 (85%) | 43/50 (86%) | | 63/73 (86%) | |
| Rao *et al.* (1978) | 92 | 24/26 (92%) | 18/21 (86%) | 10/13 (77%) | 61/73 (84%) | 8/243 (3%) (Stricture, perforation or perineal ulceration—includes 74 patients treated radically) |

It is important to note that pain is frequently relieved with radiotherapy, a symptom that cannot be addressed with laser. Tenesmus is also frequently relieved by radiotherapy.

### 2.2.2.4 Intracavitary/interstitial irradiation

As early as 1950 Cade reported treatment of low rectal cancers by intracavitary radium. More recently Papillon (1975) reported a series of 133 carefully selected patients with early mucosal lesions. All lesions were below the peritoneal reflection. Papillon used both contact X-ray and interstitial methods. The dose applied at each application was 25 to 40 Gy and repeated applications were given to a total maximum dose of 150 Gy. Rapid tumour shrinkage occurred after each application. Results were impressive, there was a 5 year survival of 78% and a cancer mortality of only 9%. Sischy (1980) reported similar results with a smaller series.
Despite the very high radiation doses employed, complications were not a major problem, mild proctitis occurring in most patients and an 8% incidence of "benign rectal wall necrosis".

In the treatment of advanced rectal cancer Papillon (1984) found this treatment far less satisfactory. Although pain and blood loss could be reduced he found a diverting colostomy was often necessary during the course of treatment. In a separate series, Puthawala (1982) treated 40 patients with advanced rectal cancer with a combination of interstitial and external beam radiotherapy. Patients were initially treated with 40 to 50 Gy of external irradiation before undergoing interstitial implants on two separate occasions. The total dose to the primary site ranged from 70 to 90 Gy. Local control was achieved in 28 patients (70%). Twenty four patients (60%) were alive with good local control after a mean follow up of 3 years. Despite the high dosage of radiotherapy in patients with advanced disease, the complication rate was low. Serious complications occurred in only 8 patients (20%). Six had soft tissue necrosis, two of whom died with haemorrhage. One patient developed an ischiorectal abscess and another a rectovaginal fistula. The authors concluded that locally extensive carcinoma of the anorectum within 8cm of the anal verge could be effectively treated by a combination of external and interstitial irradiation.

### 2.2.2.5 Electrocoagulation

This technique was introduced by Strauss (1935) and has subsequently been strongly advocated by various groups (Wittoesh 1958, Madden 1971, Crile 1972, Eisenstat 1982). Complications are recorded more frequently than experienced with laser treatment which is not surprising in view of the aggressive approach adopted. Maddan's (1983) results are typical, complications occurred in 23% of those treated. Bleeding was the most common and occurred in 16% (38/204 patients). This was severe enough to require transfusion in about half. Other serious complications occurred in 11 patients (5%), 4 developed rectovaginal fistulae, 2 suffered perforations and 5 developed rectal strictures.

Results with electrocoagulation can be impressive. Wittoesch (1958) reported a series of 128 patients technically suitable for surgery but who refused an operation or were considered medically unfit. They were treated conservatively with electrocoagulation or in a few cases irradiation or local excision, 54 survived for 5 years and of the 75 who died 24 succumbed from unrelated disease! Madden (1971) attained similar results on 77 patients. Thirty seven of 54 patients with operable lesions (71%) were alive with an average follow up of 4 years. In a subsequent paper (1983) results on 204 patients were documented. One hundred and fifty six of these patients were deemed to be operable and were treated with electrocoagulation as the primary curative method. In this group the five year survival was 62% (97 patients). Similar results were recorded by the other groups mentioned. Overall the long term local failure rate for this technique when employed with curative intent is 20-30% however one group (Hoekstra 1985) reduced this to

6% by careful selection of patients (tumour< 1/3 circumference). Most studies focus on electrocoagulation for cure but a few have included patients treated with palliative intent. Details of response of specific tumour related symptoms are often not recorded. Hoekstra however recorded good palliation in 14/18 such patients.
It is likely that this technique is as effective in palliation of advanced rectal cancer as the other techniques discussed but the necessity for anaesthesia, higher morbidity and prolonged hospitalisation are serious drawbacks.

### 2.2.2.6 Transanal Resection

Use of the urological resectoscope for inoperable carcinoma of the rectum was first described for relief of obstruction by Zinkin in 1979. Several authors have subsequently advocated the technique (Irwin 1984, Ottery 1986, Kurtz 1988). The largest of these series is only 23 patients. A recent study (Berry 1990) included 81 patients with both benign and malignant lesions and recorded the results of treatment in detail. Berry treated 54 patients with rectal adenocarcinoma and and 23 with adenomas. The predominant presenting symptoms were change in bowel habit (17 patients), rectal bleeding (9 patients) and rectal pain and tenesmus (10 patients). These were abolished or improved in 75%, 83% and 60% of patients respectively. These results were achieved with only one procedure in 52 patients and only 11 patients required three or more procedures. Of 27 patients with potentially curable cancer 21 were alive at one year post treatment.

Complications were encountered more commonly than with Nd YAG laser treatment. Haemorrhage requiring rectal packing and transfusion was required in eight patients and three patients suffered intraperitoneal perforation of the colon necessitating immediate laparotomy. Two of these patients died. When other complications are included (pelvic sepsis, rectovaginal fistula, septicaemia, rectal stricture) there were a total of 20 serious events in 137 procedures. In addition there were a total of 9 post operative deaths resulting in a 30 day mortality rate of 11.1%.

The relatively high complication rate in comparison with laser is probably related to more radical debulking. This technique may thus be more suitable for patients with extensive intraluminal bulk where multiple laser sessions are required. The necessity for general anaesthetic and hospital stay averaging 6 days after each procedure are important drawbacks.

#### 2.2.2.7 Local Excision and Cryosurgery

Several groups have pursued local excision as a curative procedure for early rectal cancer in order to reduce procedure related morbidity and mortality. Tumours up to 8cm from the anal verge can be removed by peranal excision but more proximal tumours usually require an open procedure such as the Kraske sacral approach.

A recent series from the Mayo clinic (Biggers 1986) reviewed 234 patients with adenocarcinoma of the rectum treated locally. One hundred and eighty eight underwent local excision and 46 were treated with other local methods (Fulguration, cryosurgery, laser and radiation). No clear difference in survival was noted in patients treated by these techniques. The average size of the tumours was 2.3cm (range 0.5-8cm). Results were excellent. Ninety three patients had in situ disease and in this group survival was no different to matched controls from the general population. One hundred and forty one had invasive cancers. Overall survival in this group was not as good as those with in-situ disease. The five year survival in those with well differentiated lesions was 70% against 50% moderately or poorly differentiated lesions. Patients with lesions smaller than 3 cm in diameter survived longer. The authors conclude that patients with in-situ cancer and those with well differentiated tumours less than 3 cm in diameter are best managed by local excision.

Similar results with 82 patients undergoing local excision were achieved by a German group (Heberer 1987). The criteria for patient selection were low grade tumour < 3cm, confined to rectal wall, with histologically free excisional margins. Twenty six patients were found not to fully meet the criteria after local resection and 20 went on to radical surgery. Five year survival of those treated only by local excision was 84% which was better than that of patients from the same unit undergoing anterior resection or A-P excision (76% of 354 and 73% of 317 respectively). Post operative complications were seen in 20-30% of patients undergoing a radical procedure and only 5% of those undergoing local excision. Post operative mortality was 7.3% for A-P resection 3.5% for anterior resection and zero for local excision. The locoregional recurrence rate was 7.1% (3 patients) for patients treated with local excision. Other groups (Gall 1983, Nothinger 1985 and Lock 1978) have achieved similar results in highly selected patients.

Heberer (1987) also published their results for cryosurgery in 268 patients over the same period of time (1973-1985). The technique was employed primarily for palliation in patients with advanced disease or at high risk for surgery. Thus the patient group is similar to those treated in most of the published Nd YAG laser studies. The technique is normally applied with local anaesthetic only. It is not safe to treat lesions above the peritoneal reflection. Results were divided according to the indication. Seventy seven percent of thirty one patients with small carcinomas showed a complete response to treatment. In 217 patients with advanced disease with or without metastases colostomy was still required in 20% which is considerably higher than that seen using laser. Bleeding was controlled in 2/3 of the patients in this group but perineal pain only responded in 50%. There were 3 deaths in this series from perforation sustained during treatment.

### 2.2.3 Comments

In the radiotherapy studies the average age of patients treated (particularly the early ones) was lower than in laser trials and there was often a significant proportion of early lesions or anastomotic recurrences which are likely to be smaller and respond better to treatment. Some of the studies using local techniques have specifically selected cases with early lesions in whom "cure" is aimed at (particularly the electrocoagulation and local excision studies). In general however, patients referred for laser treatment are a particularly poor prognosis group in whom other approaches have either failed or been rejected. Patients who survive for long periods in all these studies are almost exclusively those with small tumours treated aggressively with the modality concerned. It is likely that such patients include the group with early tumours in whom tumour eradication can be achieved with laser with far lower risk of serious treatment complications. It is however likely that radical external beam radiotherapy can achieve 'cure' in some patients with disease too extensive to be eradicated with laser using present technology.

Open surgery remains the treatment of choice for rectosigmoid cancer in most patients. For elderly patients with extensive local disease in whom curative surgery is not possible palliative surgery carries a very high risk and a minimally invasive treatment is appropriate. In those with distant metastases or concurrent medical conditions precluding open surgery, a minimally invasive approach is also appropriate. We have cited considerable published evidence to support the use of Nd YAG laser in these groups as a treatment which provides valuable cost effective palliation with very low morbidity and negligible mortality. It is likely that a combination of a local treatment such as Nd YAG laser with external beam radiotherapy for selected patients with advanced rectal cancer may offer superior palliation than either treatment alone and studies exploring such an approach are appropriate.

We have also cited considerable evidence that early cancers can potentially be cured by any of these techniques. The challenge is to be sure that there is no tumour involvement beyond the rectal wall. Most surgeons would advise open surgery for such lesions and this is probably the correct approach providing the individual is fit for and agrees to such an operation. Clearly if a patient is not fit for open surgery or refuses such treatment any of the minimally invasive methods discussed may be appropriate. The excellent results achieved in large numbers of patients with small lesions treated with electrocoagulation required regular systematic follow up. Such an approach is essential if any of these techniques are to be used with disease eradication in mind.

# CHAPTER 3

## COMBINED LASER AND EXTERNAL BEAM RADIOTHERAPY FOR PALLIATION OF MALIGNANT DYSPHAGIA : A PILOT STUDY

### 3.1 Aims and rationale

The major clinical problem of oesophageal and gastric cancer is profound dysphagia in the majority, leading to severe cachexia, often local discomfort and eventually aspiration pneumonia. Laser treatment offers effective tumour debulking for rapid relief of dysphagia, it can be performed as an out patient procedure, does not have systemic effects and serious complications are rare. The major drawback of laser is the need for repeated treatments every 5 weeks or so to maintain good swallowing (see chapter 2). This is because disease is left in the oesophageal wall and beyond the lumen in local nodes and thus tumour regrowth occurs fairly rapidly. Radiotherapy however has the potential for treating all the oesophageal tumour and the local regional draining sites (Tobias 1991) and thus should be complimentary to laser.

External beam radiotherapy alone relieves dysphagia slowly, often taking several weeks for maximal effect (Pearson 1978). A recent study of palliative radiotherapy (Caspers 1988) suggested that patients with relatively good swallowing enjoy improved survival over those who swallow poorly at presentation. There is thus both theoretical and clinical evidence to support the concept that a patient whose swallowing has been improved by laser recanalisation should benefit further from radiotherapy. There have, however only been a few studies (Bader 1986, Sander 1991, Renwick 1992) which have studied the combination of laser and radiotherapy, and intraluminal rather than external beam radiotherapy was used (Bader also gave external beam treatment to those with squamous cell cancers). Intraluminal radiotherapy (brachytherapy) causes superficial damage to the tumour, as there is a rapid fall off in dose with distance from the source, and is not as effective in terms of irradiating the whole tumour as external beam treatment. These studies did however report prolonged dysphagia free intervals although only the first was randomised and in this study the benefit was only seen in patients with squamous cell cancers. The pilot study was designed to answer the following questions.

1) To determine if palliative external beam radiotherapy, a more widely available and practical technique than brachytherapy, may be a promising approach in reducing the frequency of follow up procedures following laser treatment alone.

2) To determine what radiotherapy dose regime would be appropriate in these patients.

3) If the approach appeared promising to provide data to aid designing a randomised study to test the combination treatment more rigourously.

## 3.2 Methods

### 3.2.1 Patient selection

The laser unit at University College Hospital acts as a tertiary referral centre for patients suffering from malignant dysphagia who are considered unsuitable for surgery. A smaller number of patients treated with laser (around 20%) present directly to the hospital. Patients recruited into this study were initially seen by us between September 1988 and June 1989. Patients with predominantly exophytic carcinomas of the oesophagus and gastric cardia were eligible for the study. All patients recruited were deemed inoperable either due to advanced disease or unacceptable anaesthetic risk. Five patients had documented metastatic disease, five had advanced local disease detected at CT scan and 3 had undergone laparotomy and their tumours could not be resected. A further nine were considered unsuitable for surgery due to age and/or general debility. Patients with a good technical result from laser and swallowing fluids or better were assessed for radiotherapy by Dr Tobias (consultant radiotherapist) before trial entry. Those who had had previous radiotherapy were excluded. All patients had either squamous cell carcinomas of the oesophagus or adenocarcinomas of the cardia. Patients with malignancy arising in organs other than the oesophagus and causing dysphagia by direct invasion or metastatic spread were excluded. Full demographic data are given in table 3.1.

**Table 3.1**

**Patient characteristics**

| | |
|---|---|
| Total No | 22 |
| Male/Female | 15/7 |
| Mean age (yrs ± sd) | 68(11) |
| Squamous call carcinoma/Adenocarcinoma | 9/13 |
| Cardia/thoracic | 15/6 (1 anastomotic) |
| Mean tumour length (Cm sd) | 7(3) |
| Metastases | 5 |
| Inoperable- CT scan or at Laparotomy | 8 |
| Medically unfit | 9 |

### 3.2.2 Ethical aspects

All patients were instructed as to the nature of the study. Formal ethical committee approval was not considered necessary as both laser and external beam radiotherapy treatment are well established therapies for oesophageal cancer and all patients entered into the study were treated identically (no randomisation).

### 3.2.3 Techniques

Endoscopic and laser technique has been discussed in detail in chapter 1. At initial endoscopy patients underwent laser sessions as appropriate to destroy intraluminal tumour and restore oesophageal patency. Oesophageal dilatations were performed for strictures if the endoscope would not pass in order to enable full evaluation of the tumour and improve access for optimal laser treatment. All patients were irradiated using supervoltage teletherapy (cobalt 60). The target volume was determined by the length of tumour with a 5cm margin at the upper and lower border of the tumour and a 3 cm margin circumferentially. The treatment was delivered by anterior and posterior opposed fields in all cases. In the early part of the study patients were initially given 20Gy in 5 or 10 fractions and six patients who had tolerated this dose well were given a further dose 20Gy dose either immediately or 4-6 weeks later (total dose 40Gy). It soon became apparent that most of these patients could not tolerate this total dose and subsequent patients all received 30Gy in 10 fractions. Twenty patients had to stay in hospital for DXRT. This increased the median lifetime total hospital stay to 21 days in comparison to historical in-patient times of around 14 days for laser only.

### 3.2.4 Follow-up

All patients underwent follow up endoscopy three weeks after completion of radiotherapy (check endoscopy). Endoscopic findings were recorded as at initial endoscopy, and further laser treatment was applied only to polypoid tumour. All patients were subsequently contacted monthly by the research sister, Sally Thorpe, to assess progress and the necessity for further treatment. Dysphagia score was recorded according to the scale previously used by us { 0=normal; 1=most solids; 2= semi solids; 3 =liquids only ;4=difficulty with liquids}. Patients whose dysphagia grade deteriorated by one or more or who felt that their swallowing had deteriorated significantly were re-endoscoped for assessment and further therapy as appropriate.

### 3.2.5 Statistical methods

Proportions were tested using Chi squared test with Yate's correction and survival curves with the Log Rank test.

## 3.3 Results

### 3.3.1 Dysphagia grades

The median dysphagia grade for all patients prior to laser was 3 (liquids only) and this improved to a median of 1 (most solids) following laser treatment. The spectrum of dysphagia at presentation was very similar in patients treated with radiotherapy at the 30Gy and 40Gy dosage levels. Following radiotherapy there was very little change in dysphagia grades in the group treated with 30Gy but 3 of the 6 receiving 40Gy showed a marked deterioration and swallowed only fluids to death. Regarding a mean dysphagia grade of 2 (semi solid diet) for the duration of each patients survival as a success, 14/16 in the 30Gy group and 2/6 in the 40Gy group enjoyed a successful outcome. This difference is significant at the 5% level (Chi squared test).

Three patients entered into this study were swallowing only fluids after initial laser recanalisation. One received the higher radiotherapy dose. Although radiotherapy was tolerated well by 2 of them swallowing did not improve with treatment. One was eventually intubated and the other 2 enjoyed only short survival (8 and 9 weeks respectively).

### 3.3.2 Dysphagia controlled interval (DCI) and further therapy

The dysphagia controlled interval is the time between the 'check' endoscopy and the next performed when an individual suffered further deterioration of swallowing or to death. The figures for all patients broken down according to histology and radiotherapy dosage are shown in table 3.2 and data from historical laser only patients (Loizou 1991) are also given. Overall, patients treated with radiotherapy have a DCI of 9 weeks (median) and for patients receiving the 30Gy dose this is slightly longer (13 weeks). The DCI was longer for patients with squamous cell carcinomas than adenocarcinomas (17 weeks v 13 weeks).

Eleven patients required no further treatment after check endoscopy (one still alive after 4 years) and the median survival in this group was 9 weeks. Considering all those who required further endoscopic treatment after the check endoscopy the median interval between follow up procedures required was 13 weeks (range 4-67). Eight patients required dilatation at check endoscopy but only 3 of these had fibrous strictures only, the rest having regrowth of tumour as well. Overall, 13 patients required further endoscopic treatment for tumour following DXRT. Three patients who developed severe dysphagia from extrinsic strictures were intubated (at 5 weeks, 5 months and 14 months after start of treatment). All swallowed well with tubes (dysphagia grade 2). Two survived several more months but the third died a few weeks after intubation. All but one of the patients have died at the time of writing. None died of aspiration, all gradually weakened with cancer cachexia and/or the effects of metastatic disease.

**Table 3.2 Dysphagia controlled interval (DCI) in weeks after 'check' endoscopy**

| | Squamous cell carcinomas | Adeno carcinomas | All patients |
|---|---|---|---|
| All patients median(range) | 17 (1-200) weeks | 9 (2-26) weeks | 9 (1-200) weeks |
| 30 Gy dose only | 20 (3-200) weeks | 11 (2-23) weeks | 13 (2-200) weeks |
| Historical laser only controls | 5 weeks | 5 weeks | 5 weeks |

### 3.3.3 Survival

This study was not set up to assess survival however it became apparent that some patients in the 30 Gy group were living for considerable periods and so survival data was examined further. Table 3.3 shows the crude survival data from presentation for each group receiving radiotherapy and for historical laser only controls again taken from our earlier study (Loizou 1991). This data gives the impression of improved survival in the 30Gy group and survival curves were plotted (figures 3.1 and 3.2). There is a significantly prolonged survival in the group receiving the 30Gy dose over historical controls ($p<0.025$). As the study was not randomised it could reasonably be argued that this difference is at least partly due to differences in selection. There was no significant difference between the groups receiving different doses of radiotherapy although the survival of patients receiving 40Gy is generally shorter. One patient in the 30Gy group is still alive. She is a 78 year old who presented with a 3cm squamous cell cancer and has remained well for 4 years with entirely normal swallowing since treatment at 3 laser sessions followed by the radiotherapy.

**Table 3.3 Survival data according to subgroup**

| | Laser+30Gy | Laser+40Gy | Laser Only |
|---|---|---|---|
| Patient No | 16 | 6 | 43 |
| Median Survival (range) | 44(8-205*) | 19(7-73) | 22(4-117) |
| 1yr survivers | 5/16 (30%) | 1/6 (16%) | 5/43 (12%) |

*1 patient still alive at 205 weeks

**Figure 3.1 Survival curves laser + 30 Gy and historical laser only controls**

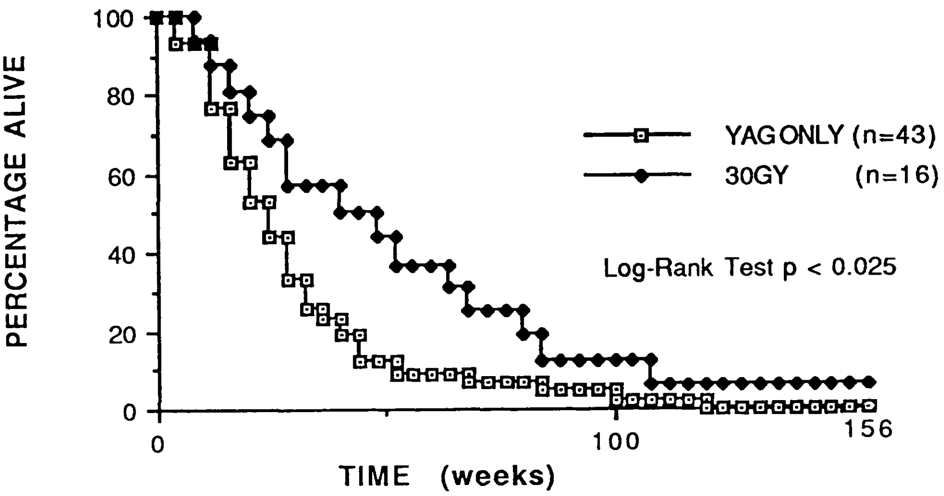
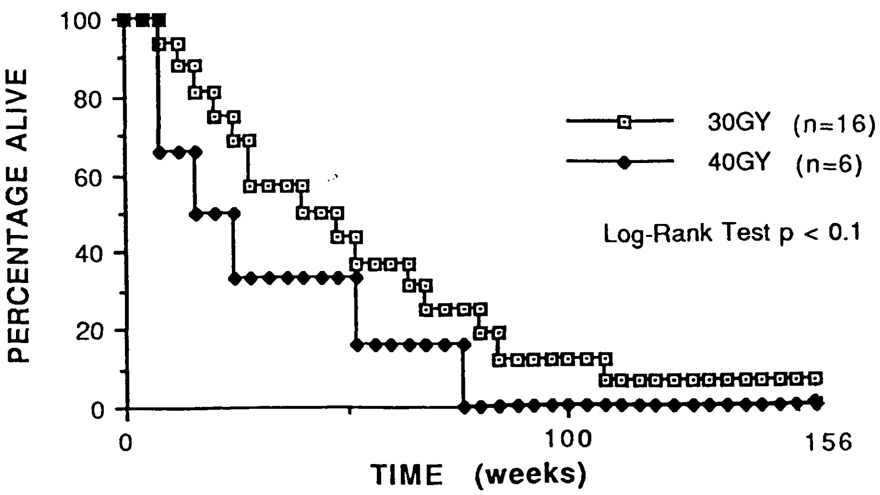



**Figure 3.2 Survival curves laser + 30 Gy and laser + 40 Gy**



### 3.3.4 Complications

No perforations were experienced in this group of patients. Mild nausea, lethargy and odonyphagia were common during radiotherapy but usually did not amount to more than a minor irritation for most patients. Radiotherapy was poorly tolerated in 3 of the 6 patients who received the higher radiotherapy dose. They never really recovered following radiation, most did not swallow well and succumbed fairly rapidly from cancer cachexia. Only 2 of the 16 who received the 30Gy dose had more than minor symptoms. One of these succumbed early with poor swallowing but the other recovered and eventually died swallowing well 24 weeks after treatment.

Fibrous strictures were identified in 3 patients at the 'check' endoscopy and another 5 had fibrous narrowing as well as further luminal tumour growth. Two of those with fibrous strictures required no further treatment after dilatation at the 'check' procedure and the third needed dilations every 9 weeks for a year.

## 3.4 Discussion

This study was designed to give an indication whether the theoretically attractive combination of laser and external beam radiotherapy may be useful in the clinical setting and if so at what dose. More specifically the hope was to combine the better palliation of dysphagia achievable with laser with the more prolonged relief normally only achievable in the palliative setting with a tube. The results look promising, although 50% of patients require follow up procedures after the 'check' endoscopy the frequency of these appears to be reduced quite dramatically in comparison to historical control data.

As these patients were receiving palliative treatment it is important not to be so aggressive that the side effects of radiotherapy detract significantly from the benefit achieved with laser either in terms of deterioration in general condition or dysphagia. The results indicate that the 30Gy dose in 10 fractions is well tolerated in this patient group. Our limited experience of higher doses in this palliative setting is not favourable although the numbers treated were small. Overall the dysphagia controlled interval is prolonged and subsequent necessity for follow up endoscopy is reduced, particularly for squamous cell cancers in comparison to historical control data. It is of interest that the one controlled brachytherapy study mentioned (Sander 1991) also demonstrated a prolonged dysphagia free interval but only for patients with squamous cell tumours. One concern of applying 2 treatments which can induce fibrosis was that we would have an unacceptable number of fibrous strictures but that was not the case. Only 3 patients came back with sole 'fibrous' narrowing at the check endoscopy and all of these were easily dilateable at the same procedure. Overall 13 patients required further laser for tumour after external beam radiotherapy. This suggests that the radiotherapy may be slowing tumour regrowth rather than causing wholesale tumour necrosis.

The survival curves for the 30Gy group and 43 historical controls indicate the possibility of increased survival with external beam radiotherapy. However it is important to treat comparisons with historical data with caution in view of possible differences in patient selection.

The results of this pilot study are promising and indicate that a randomised study to evaluate the combination of laser and external beam radiotherapy at the 30Gy dose in 10 fractions in a larger number of patients would be worthwhile. Such a study has been performed and is discussed in the next chapter.

# CHAPTER 4

## COMBINED LASER AND EXTERNAL BEAM RADIOTHERAPY FOR PALLIATION OF MALIGNANT DYSPHAGIA : A RANDOMISED STUDY

### 4.1 Aims and rationale

Although the pilot study indicated that additional radiotherapy at an appropriate dosage was helpful the results of any study which relies on historical controls needs testing on a randomised basis. This randomised study was initiated to determine whether palliative external beam radiotherapy at the dose shown to cause minimal distress to these seriously ill patients may reduce the the need for frequent follow up procedures compared with laser treatment alone.

#### 4.1.1 Sample size estimation

Sample size estimation is undertaken to determine the number of patients which need to be studied to detect a worthwhile effect, if it exists, and to be reasonably sure that no benefit exists if it is not detected. The parameter we chose to assess is the time from check endoscopy to the next therapeutic procedure (or dysphagia controlled interval). There are four components required for sample size estimation (Altman 1982). For the purposes of this assessment we have assumed the variables are normally distributed (the plotted data for 'check' to first repeat approximates to normal distribution).

#### 4.1.2 Significance level

This is the probability of rejecting the null hypothesis when it is true. Usually a figure of $p < 0.05$ is taken as indication that the null hypothesis should be rejected (the treatments are different).

### 4.1.3 Power

This is the probability of rejecting the null hypothesis when it is false. (The probability of rejecting the null hypothesis of no difference between treatments when there is a treatment difference). It is common to accept a power of 85% for sample size calculations.

### 4.1.4 An estimate of the variability of the response variable (S)

This was calculated using data from the pilot study and from historical laser only control patients. The standard deviation of check to first repeat for those receiving 30 Gy was 9 weeks (excluding one patient who was probably cured with radiotherapy) and for those treated with laser only 3.3 weeks. Using the formula for the combined estimate of the variance used in the t test (Altman 1982)

S = 5.5.

### 4.1.5 The clinically relevant difference in treatments (CD)

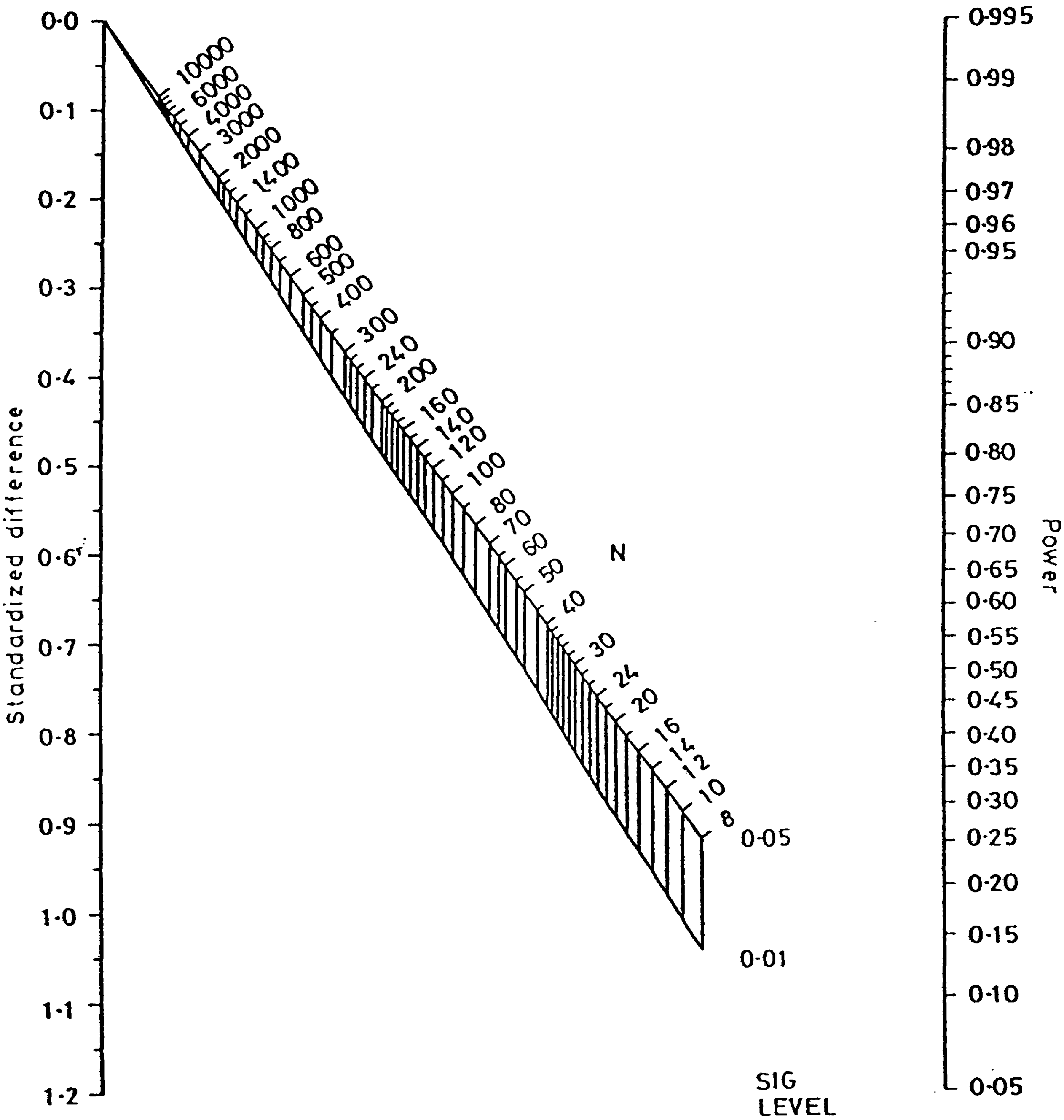
This is the difference that would be clinically valuable and we would not want to overlook. We estimate this to be 5 weeks (ie a doubling of time from 'check to repeat')

### 4.1.6 Calculating sample size

The standardised difference (**D=CD/S**) is calculated. Thus **D = 5/5.5 = 0.91.** Using a nomogram from Altman 1982 for a 2 sample comparison of a continuous variable, relating power, total study size, standardised difference, and significance level and assuming a power of 85% is required and the significance level required is 0.05 then N=45, so a minimum of 23 patients are required in each group (figure 4.1)

**Figure 4.1**

Nomogram for calculation of sample size (Altman 1982).




Nomogram for a two-sample comparison of a continuous variable, relating power, total study size, the standardised difference, and significance level.

## 4.2 Methods

### 4.2.1 Patient selection

The patients entered into this study were recruited from patients presenting at or referred to UCH between January 1990 and May 1992. They were a similar spectrum of patients to those entered in the pilot study. Twenty seven patients had squamous cell carcinomas of the oesophagus and 40 adenocarcinomas of the cardia. None had previously received radiotherapy or chemotherapy. Patients with malignancy arising in organs other than the oesophagus or gastric cardia and causing dysphagia by direct invasion or metastatic spread were excluded.
Patients with dysphagia scores of 3 or worse despite removal of as much tumour as possible with laser were not considered for this study but were intubated as similar patients had not done well with radiotherapy in the pilot study. Abdominal ultrasound was performed in all patients and 59 patients underwent endoluminal ultrasound after initial recanalisation.

Twenty four patients (36%) were over 75 years, a figure which is comparable with the overall incidence in England and Wales but higher than in other hospital series (Earlam 1990). Demographic data according to randomisation is given in tables 4.1 and 4.2. The distribution of patient characteristics in the two groups was very similar. Fourteen patients had documented metastatic disease and 13 known advanced local disease (4 detected at CT scan, 2 unresectable at laparotomy, the remainder endoscopically large tumours of which 12 of 13 were subsequently found to be stage 3 tumours on endoluminal ultrasound). The remaining 40 patients were considered unsuitable for surgery due to age and/or general debility or coexistent medical conditions (mainly cardiopulmonary) which were considered to confer an unacceptable surgical risk. Eight of these 40 (4 in each arm) had anastomotic recurrences.

**Table 4.1 Demographic details of laser and laser with radiotherapy groups**

| | *Laser only (n=30)* | *Laser + DXRT (n=37)* |
|---|---|---|
| *Sex M/F* | 20/10 | 26/11 |
| *Age median (range)* | 71 (55-88) yrs | 72 (50-85) yrs |
| *Metastases* | 8 (27%) | 6 (16%) |
| *Known extensive local disease* | 5 (17%) | 8 (22%) |
| *SCC/ANC* | 12/18 | 15/22 |
| *Tumour length median (range)* | 7 (3-17) cm | 6 (2-16) cm |
| *Symptom duration* median (range)* | 3 (1-12) months | 3 (1-12) months |

* reliable data on 55/67 patients
SCC= Squamous cell cancers
ANC= Adenocarcinomas

**Table 4.2 Tumour details of laser and laser with radiotherapy groups**

| | *Laser only* | *Laser+DXRT* |
|---|---|---|
| ***Tumour location*** | | |
| *Cervical* | *0* | *2 (All SCC)* |
| *TO {Upper/Lower}* | *10 (All SCC) {4/6}* | *10 (All SCC) {1/9}* |
| *Cardia ± lower TO* | *20 (18 ANC, 2 SCC)* | *25 (22 ANC, 3 SCC)* |

*TO = Thoracic oesophagus*
*ANC=Adenocarcinoma*
*SCC= Squamous cell carcinoma*

### 4.2.2 Ethical aspects, randomisation and administration

The study was designed and organised by the author. Formal approval was obtained from the local hospital ethical committee. Consent was also obtained from referring physicians or surgeons prior to inclusion of their patients. Once a suitable patient had reached the dysphagia criteria (semi-solid diet) following laser recanalisation, the study details were explained by the author and Sally Thorpe (the research sister) returned to the patient later to ensure that the details had been fully understood. An approved patient information sheet was also provided to patients considered for the study. Only patients giving full informed consent were considered. They were then seen by the consultant radiotherapist (Dr Tobias) to assess fitness for radiotherapy. Those deemed fit were stratified according to histology before randomisation by sealed envelopes. Early in the study 3 patients with adenocarcinomas of the cardia randomised to receive radiotherapy were subsequently considered unfit, two before treatment was started and one who had received only 2 fractions. In addition to these 3 patients one patient in the laser only arm subsequently requested and was given radiotherapy shortly after 'check' endoscopy. All patients randomised are included in the analysis on an 'intention to treat' basis.

### 4.2.3 Techniques

#### 4.2.3.1 Therapeutic

The laser technique has been dealt with in detail in chapter 1. All patients randomised to external beam radiotherapy were irradiated using the same techniques and parameters as in the pilot study. Patients were given 30Gy in 10 fractions over 2 weeks which was the dose best tolerated with apparent success in the pilot study.

#### 4.2.3.2 Endoluminal Ultrasound

Examinations were performed following laser recanalisation in order to ensure passage of the probe beyond tumour. In many cases ultrasound was performed at the same procedure as therapeutic endoscopy and under the same sedation. Diazemuls alone was used as sedation in those patients not undergoing therapeutic procedures. An Aloka 5 MHz curved linear array probe was used in this study (Figure 4.2). It is almost square in cross section and can be steered in one plane at 5 cm from the tip. It connects directly to a standard Aloka SSD 650 ultrasound console. It is significantly narrower (8mm v 13mm) than the standard Olympus endoscopic ultrasound probe which allows direct vision of the lesion and gives a circumferential view. The probe is passed blindly into the oesophagus and down to tumour level and beyond. At each level it was necessary to rotate the probe through 360 degrees to image the tumour through all 4 quadrants. Hard copies were obtained of the areas of maximal wall thickness, of tumour infiltration into surrounding tissues and of lymph nodes. The intention was to perform examinations on as many patients as possible after initial recanalisation and again at 'check' endoscopy in order to assess the change in tumour bulk in those who did and did not receive radiotherapy. Fifty nine patients underwent an endoluminal ultrasound examination following initial laser recanalisation and 42 of them had a second procedure after appropriate treatment at the 'check endoscopy'.

Figure 4.2 i) The Aloka 5Mz curved linear array probe

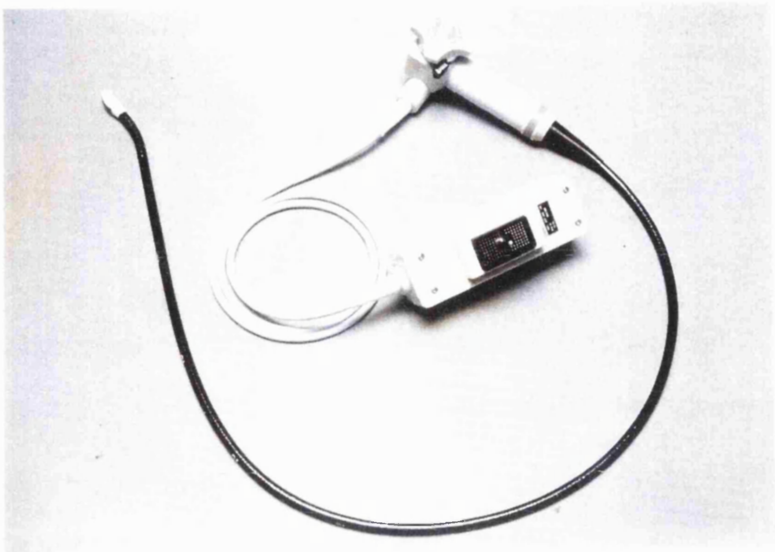


Figure 4.2 ii) Close up wiew of the curvilinear transducer showing tip deflection.

#### 4.2.3.4 Follow-up

All patients underwent a 'check' endoscopy five weeks after initial recanalisation (3 weeks after completion of radiotherapy in those receiving it). At that time endoscopic therapy was given as appropriate (laser for polypoid tumour, dilatation for stricture) and endoluminal ultrasound examination was repeated if practicable. All patients were provided with telephone access to the research nurse and given instructions to phone if they noticed deterioration in swallowing. In addition all patients were contacted monthly to assess progress, and record dysphagia grade. If this deteriorated by one grade or more patients were re-endoscoped for assessment and further therapy as appropriate. Patients who were having difficulty managing a semi-solid diet for most of the time were intubated with celestin tubes (4).

#### 4.2.3.5 Statistical methods

Statistical analysis was performed using the Wilcoxon Rank sum test for intervals between treatments, the Wilcoxon signed rank test for paired ultrasound data, Chi squared test with Yate's correction (for proportions) and the Log Rank test for survival. The unpaired t test was also used for 'check' to repeat data.

## 4.3 Results

### 4.3.1 Hospital stay

The median treatment related lifetime hospital stay for those receiving radiotherapy was 19 days (range 3-53) and 14 days (range 0-28) for those treated with laser only.

### 4.3.2 Dysphagia

A dysphagia grade of 2 or better after initial laser recanalisation was required for entry into this study. In the event the swallowing of all but 5 of the patients entered had improved by at least one dysphagia grade after initial recanalisation. The grades for each arm of the study are given at each stage in figure 4.4. The median dysphagia grade improved from 3 to 1 and almost 60% of patients were swallowing some solids for most of their lives. Comparing the proportion of patients benefiting from dysphagia grades 0 or 1 after treatment with those with grades or 2 or 3 there is no significant difference between the laser + radiotherapy and laser only groups at any stage (Chi squared test with Yate's correction).

### 4.3.3 'Dysphagia controlled interval' and 'treatment interval'

The initial 'dysphagia controlled interval' (DCI) or 'check' to first repeat was the duration of time between the 'check' endoscopy and the next follow up procedure, performed when the patient complained of further deterioration in swallowing or to death if a further procedure was not required. The figures for all patients according to histology and treatment arm are given in table 4.3 and DCI data are shown graphically in figure 4.4. Overall the DCI in the laser only group was 5 weeks and 9 weeks in those also receiving radiotherapy. This difference was significant at the 5% level (Wilcoxon rank sum) for all patients and for each histological group taken alone. Using the unpaired t test this difference was significant at the 1% level for all patients and for adenocarcinomas only but not for squamous cell cancers only. Eight patients who did not survive long enough to have a 'check' endoscopy of whom 3 were in the radiotherapy group are excluded from this analysis.

**Figure 4.3 Dysphagia grades with time for all patients**

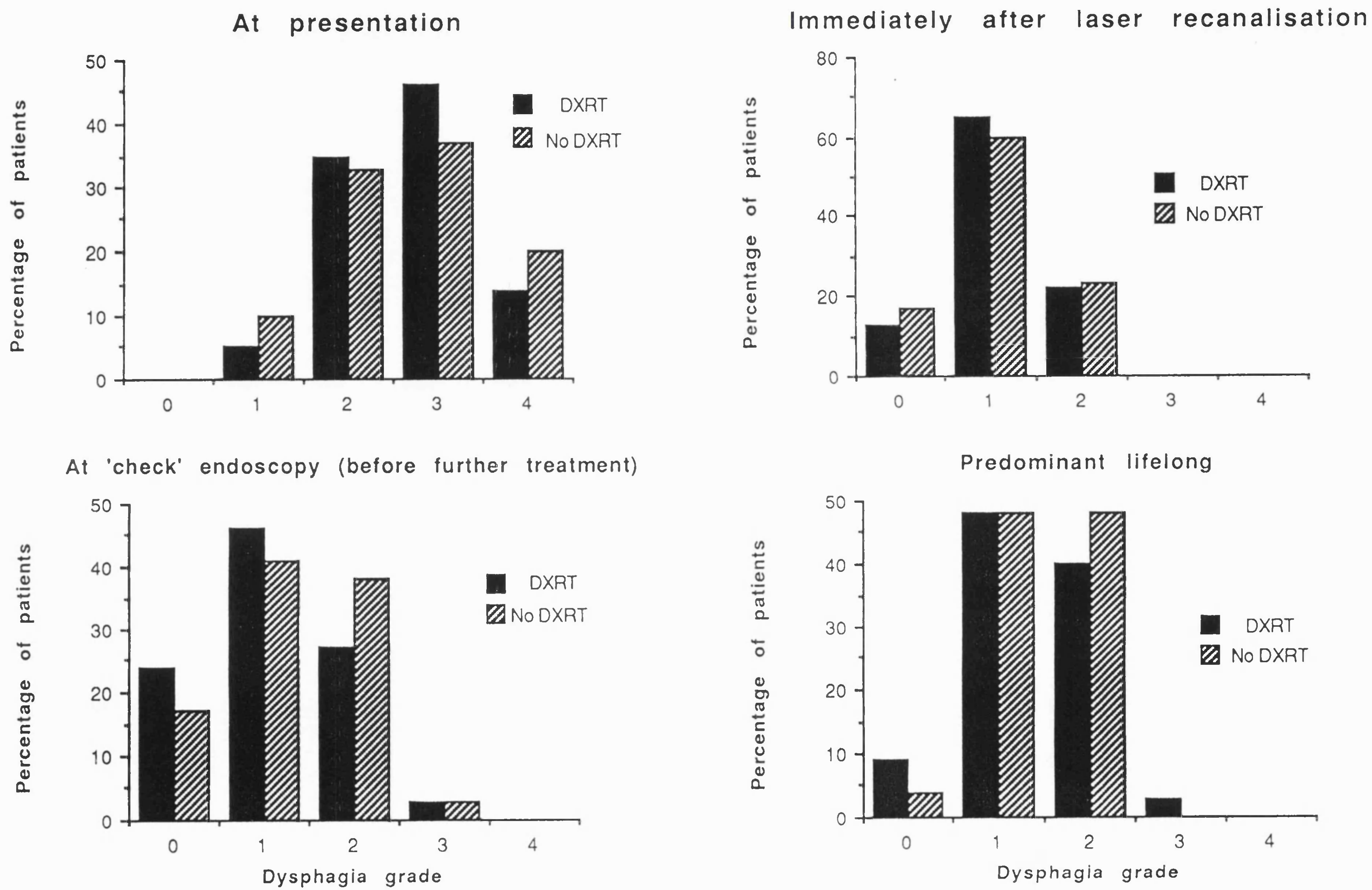


**Table 4.3 Frequency of therapeutic endoscopy required to control symptoms according to histology and randomisation group**

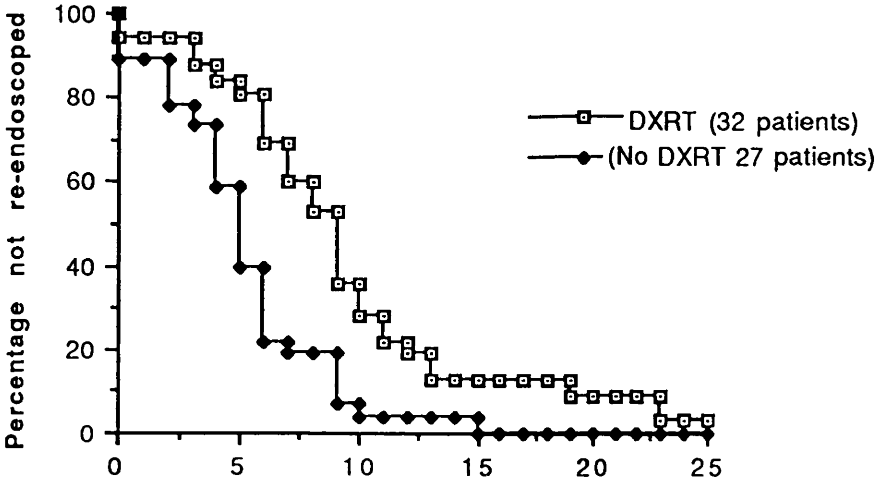
| | *Squamous cell cancers* | | *Adenocarcinomas* | |
|---|---|---|---|---|
| | *Laser* | *Laser + DXRT* | *Laser* | *Laser + DXRT* |
| Number of patients | 11 | 15 | 16 | 17 |
| ***'check' to repeat*** | | | | |
| Median | 5 | 9 | 5 | 8.5 |
| Mean | 5.0 | 9.2 | 5.3 | 11.0 |
| (range) *in weeks* | (0-10) | (0-24) | (0-15) | (3-48) |
| ***treatment interval*** | | | | |
| Median | 6 | 10 | 4.5 | 7 |
| Mean | 5.5 | 10.0 | 5.5 | 8.6 |
| (range) *in weeks* | (0-12) | (0-25) | (1-15) | (3-23) |

A) Comparing laser alone with laser +DXRT (Wilcoxon Rank Sum)
i) All patients and adenocarcinomas alone $p < 0.01$ for check to first repeat and treatment interval
ii) Squamous cell carcinomas $p < 0.05$ but $> 0.01$ for check to first repeat and p=ns for treatment interval

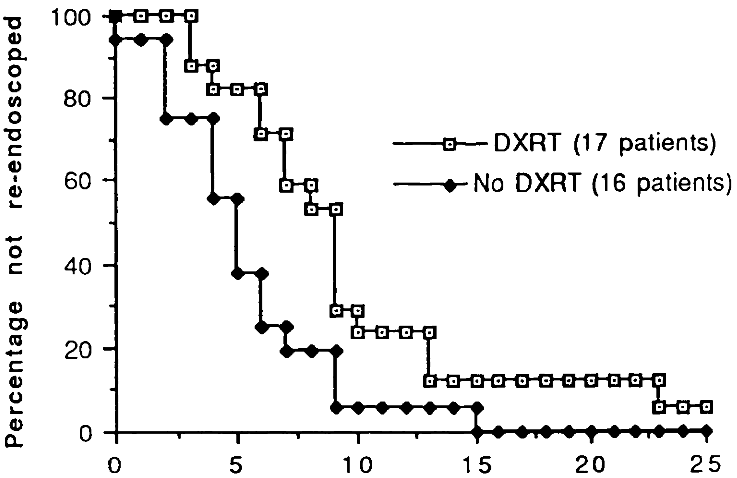
B) Comparing Adenocarcinomas and Squamous cell carcinomas (Wilcoxon Rank Sum)
i) Receiving DXRT p=ns for check to first repeat and treatment interval
ii) Not receiving DXRT p=ns for check to first repeat and treatment interval

## Figure 4.4

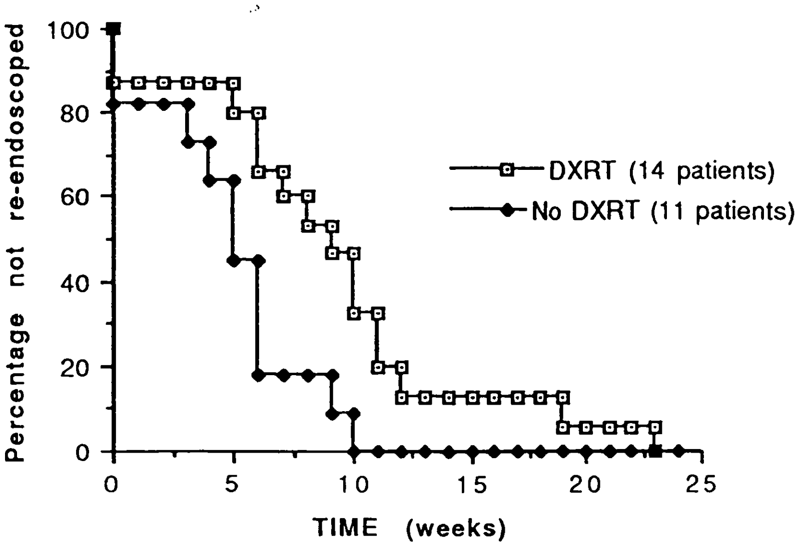
'Check' to first repeat (All patients)




'Check' to first repeat (Adenocarcinomas only)




'Check' to first repeat (Squamous cell cancers only)



The treatment interval was defined as the mean time between hospital attendance for procedures after 'check' endoscopy for the remainder of the patients life or until intubation. Overall this was also 5 weeks in the laser only group and 9 in those also receiving radiotherapy. The difference was significant for all patients and for adenocarcinomas only but not for squamous cell cancers alone (probably due to small numbers, see table 4.3). The treatment interval was longer for squamous cell cancers than for adenocarcinomas but the difference was not quite statistically significant at the 5% level, again probably due to smaller patient numbers.

### 4.3.4 Endoluminal Ultrasound

Staging was performed using the Aloka 5 MHz curved linear array probe endoluminal ultrasound shown in figure 4.4. It was also used in as many patients as possible to monitor response to radiotherapy. A deliberate decision was made not to perform CT scans as the data discussed in chapter 2 suggests that endoluminal ultrasound alone is the best technique for assessing local tumour. Follow up assessments were also performed in the control laser only group as often as possible. As discussed in chapter 2 endoluminal ultrasound is excellent at defining depth of penetration, local nodes and diagnosing direct infiltration of adjacent structures. We therefore elected to measure maximum oesophageal wall thickness and maximum size of nodes with malignant characteristics. Images demonstrating some of these aspects are shown in Figure 4.5.

It was usually necessary to perform ultrasound immediately after laser treatment or dilatation as delay would have resulted in prolonging hospital admission specifically for the examination and this was not deemed acceptable. Of 59 initial examinations 37 were performed after laser and 2 after dilatation and of 42 examinations at 'check' endoscopy 22 were performed after laser and 8 after dilatation. Performing examinations after laser may result in an exaggeration of oesophageal wall thickness due to swelling and therefore the response to radiotherapy was assessed on lymph node size and not oesophageal wall thickness.

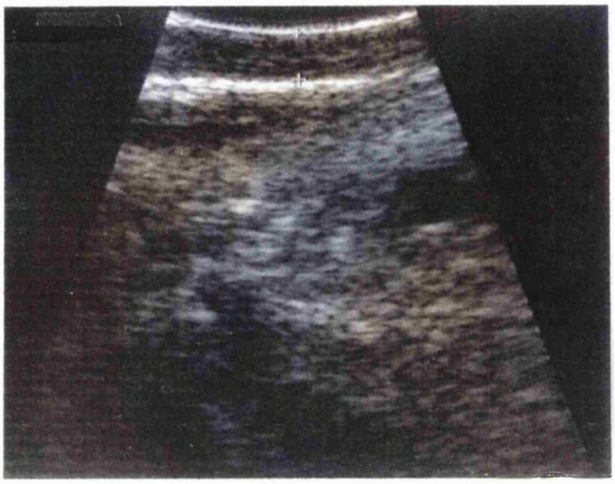
The Aloka probe could not be passed in 2 patients, one with a pharyngeal pouch and another with a cervical tumour. Occasionally the probe would not pass a stricture but after waiting for swelling to settle and/or further laser treatment we usually managed to perform a complete endoluminal examination.

Initial examination was performed in 59 patients, all were found to have full thickness oesophageal involvement. Forty four (75%) were found to have nodes which demonstrated malignant characteristics (hypoechoic pattern with clearly delineated boundaries). Details of initial ultrasound and repeat ultrasound in 42 patients at 'check' endoscopy are given in table 4.5. There is little change in maximum oesophageal wall thickness for either group between the 2 scans.

The node size does fall slightly in those receiving radiotherapy and increase slightly in those treated with laser only but comparing all parameters for the 42 patients in whom ultrasound was repeated (Wilcoxon signed rank test) this difference is not significant. Of thirteen patients with nodes greater than 1 cm diameter three (23%) showed a reduction of node size of 50% or more (2 adenocarcinomas 1 squamous cell cancer). Paired scans in those who did not receive radiotherapy showed no reduction in node size using the same criteria. Examples of sequential scans are shown in figure 4.6.

Figure 4.5 Endoluminal ultrasound images

i) Normal oesophageal wall



ii) Area of transition between normal oesophageal wall and thickened diseased oesophageal wall

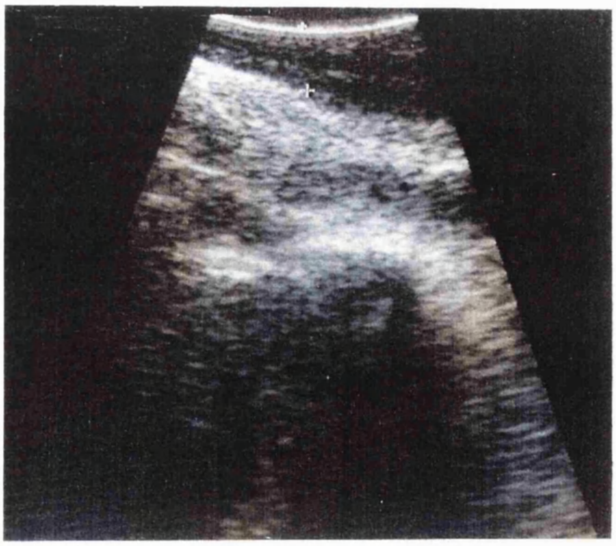
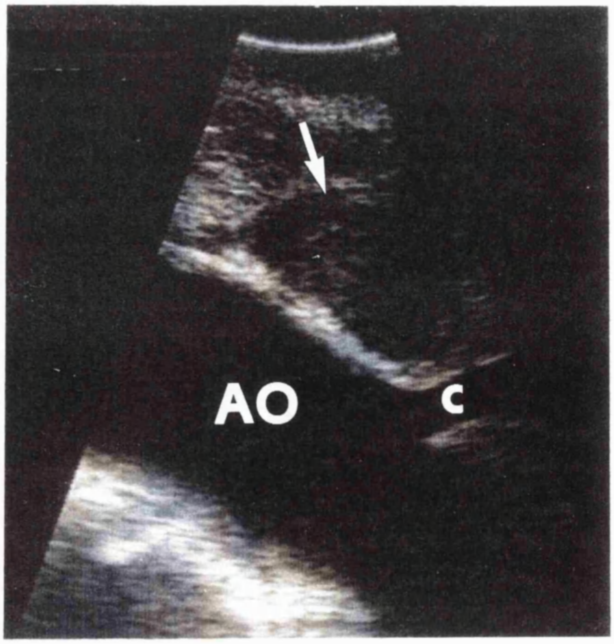


Figure 4.5 iii)

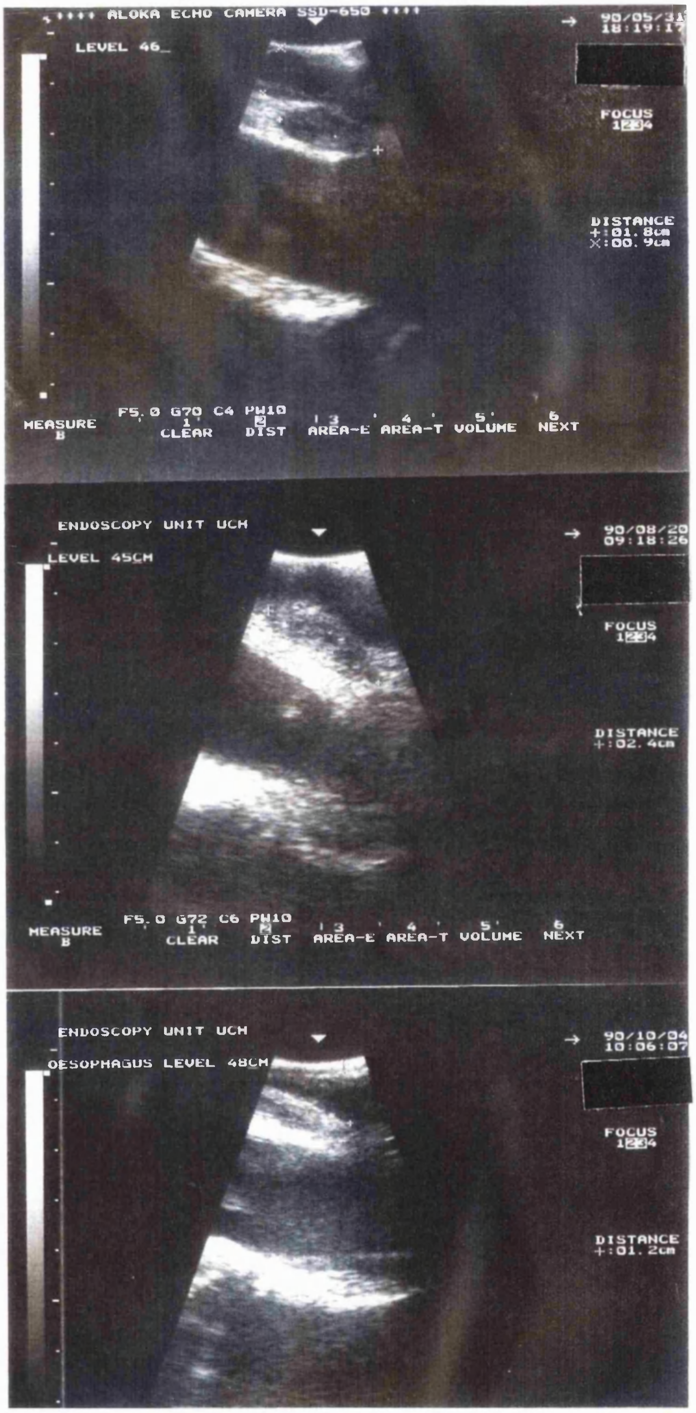
Two discrete coeliac nodal metastases


Figure 4.5 iv)

A 2cm lymph node lying superior to the celiac axis (C) and anterior to the abdominal aorta (AO)

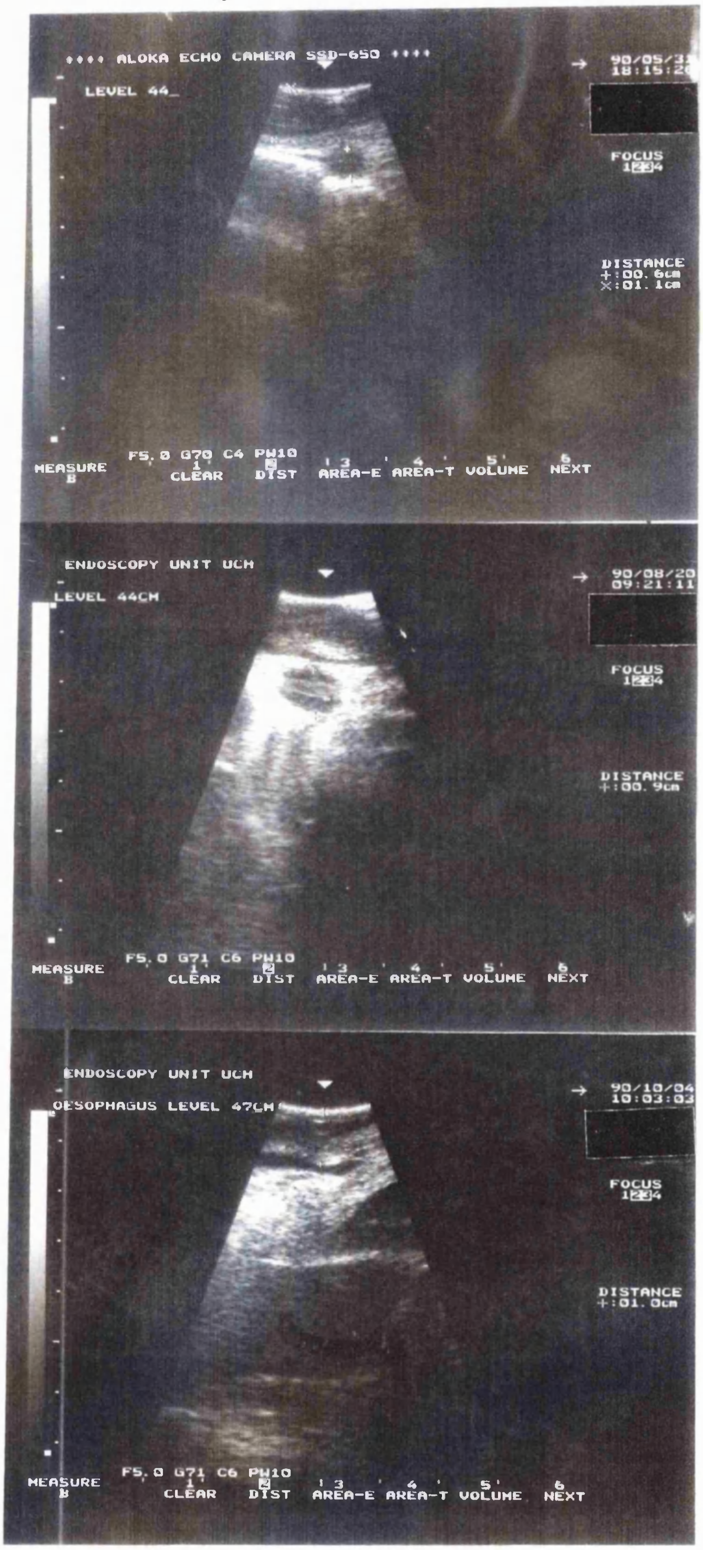


## Figure 4.6 A i Sequential endoluminal ultrasound images



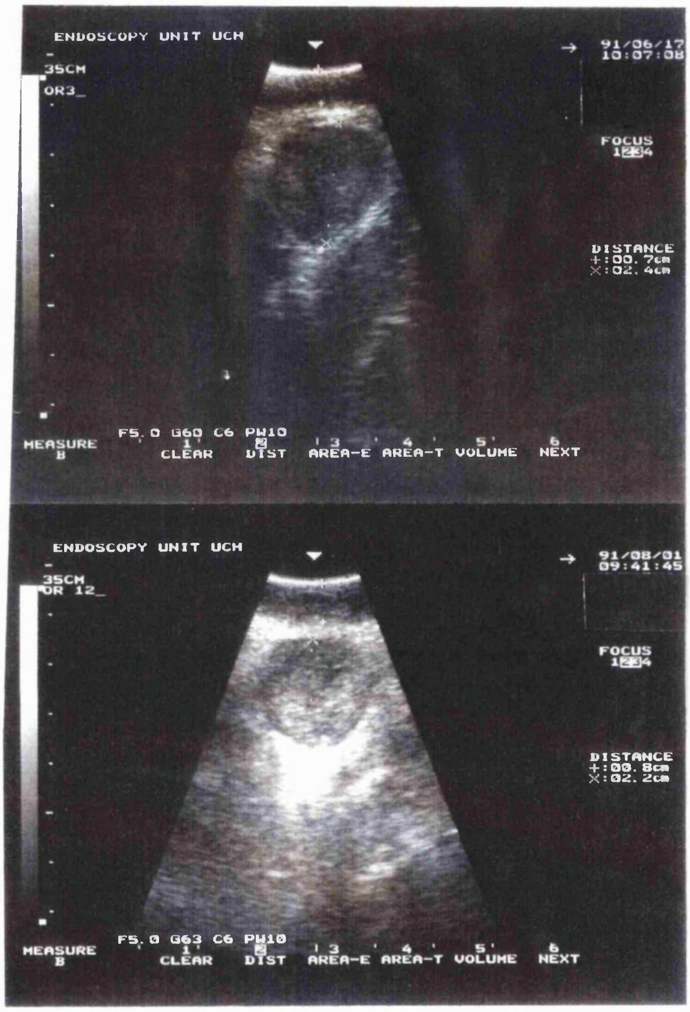

Images show a node lying in front of the aorta in a 66 year old man with adenocarcinoma of the cardia (index case no 22). The first picture was taken 2 months before laser was commenced when the ultrasound was undertaken for staging with a view to surgery. The second was taken at randomisation and the third at 'check' endoscopy following radiotherapy. The node doubled in size in 2 months but after DXRT shrank by 50% to smaller size than at the original assessment.

## Figure 4.6 A ii Sequential endoluminal ultrasound images



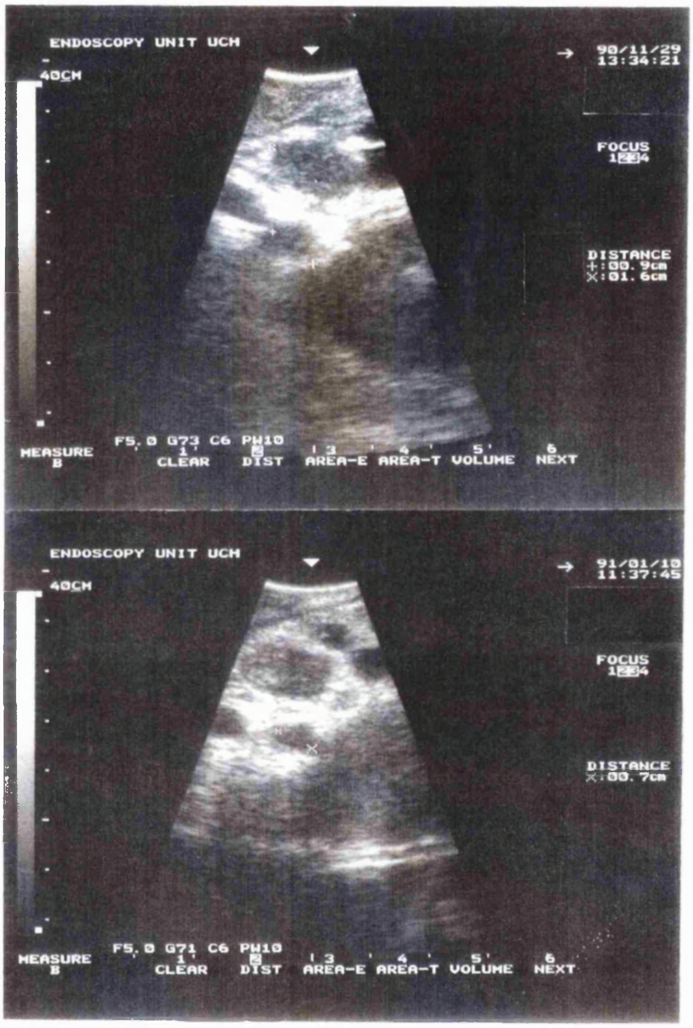

Serial Images of a second node in the same patient as figure 46 A i. The node has grown in size in the 3 months following the first ultrasound but disappeared after DXRT.

## Figure 4.6 B Sequential endoluminal ultrasound images




Images of a cardia tumour in a 74 year old man (appendix patient no 33) before radiotherapy and at 'check' endoscopy. There is a small reduction in node size after radiotherapy

## Figure 4.6 C Sequential endoluminal ultrasound images




Images of a lower thoracic tumour in a 78 year old man (appendix patient no 49) after racanalisation and again at 'check' endoscopy (no radiotherapy given). There is little change in node size.

**Table 4.4 Endoluminal ultrasound data**

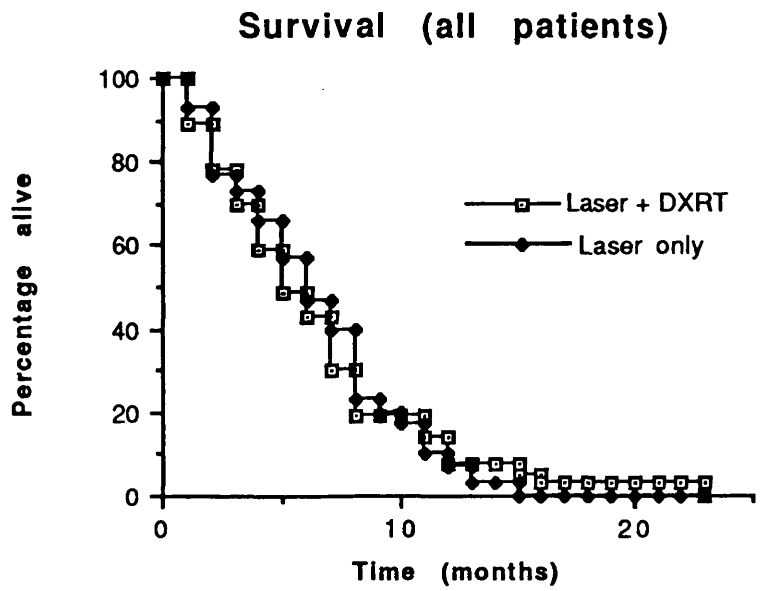
| | US One<br>Maximum thickness medium (range) | US Two<br>Maximum thickness medium (range) |
|---|---|---|
| *Oesophageal wall DXRT group (22)* | *1.6(0.8-2.4)cm* | *1.6 (0.6-3.2)cm* |
| *Oesophageal wall Laser only group (20)* | *1.5 (1.0-4.2)cm* | *1.7 (1.0-3.2)cm* |
| *Para-oesophageal nodes DXRT group* | *14/22 patients 1.2 (0.7-2.4)cm* | *16/22 patients 0.9(0.5-2.3)cm* |
| *Para-oesophageal nodes Laser only group* | *16/20 patients 1.0(0.5-1.9)cm* | *14/20 patients 1.3(0.8-1.8)cm* |

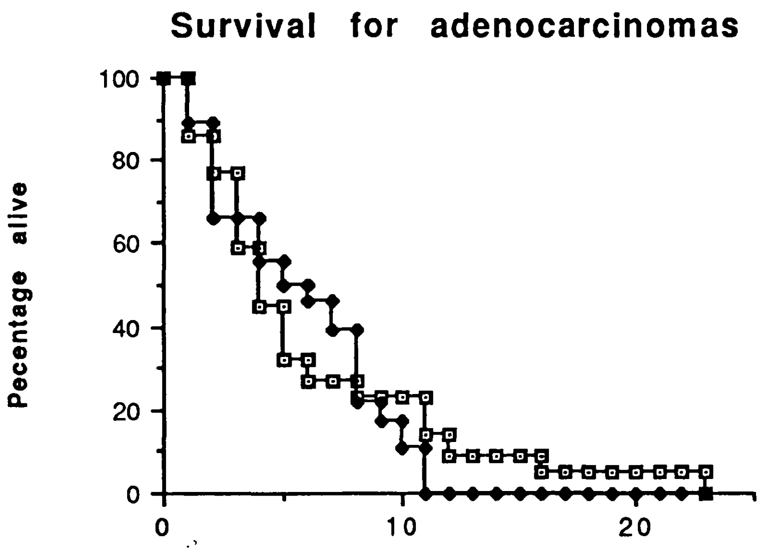
*(Data from 42 patients initially and at 'check' endoscopy)*

### 4.3.5 Survival

All the patients in this study have now died. Survival curves have been plotted for all patients and for each histological group separately (figure 4.7). These curves are remarkably similar for those treated with laser only and those also receiving radiotherapy. There is no significant difference between equivalent groups with or without radiotherapy (Log Rank test). A detailed breakdown of survival for patients with Metastases and bulky tumours is shown in table 4.5.

Figure 4.7 Survival curves according to histology and trial arm



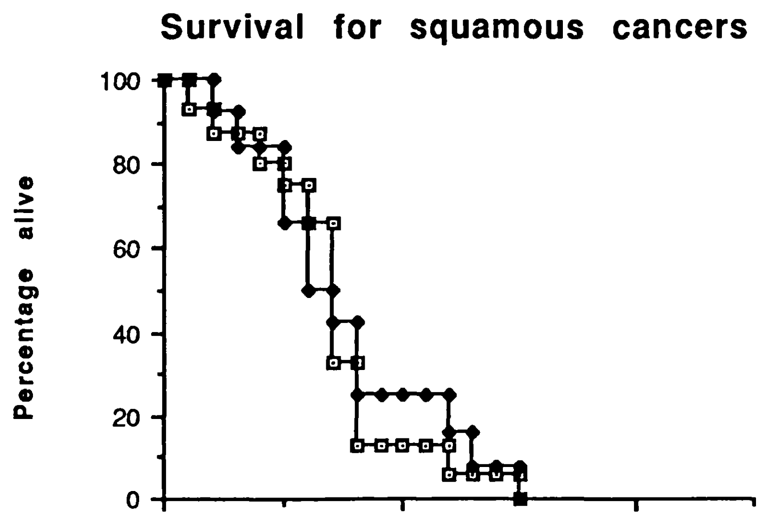



**Table 4.5 Subgroup survival**

in weeks-median (range)

| | *Laser only* | *Laser and Radiotherapy* | *Both groups* |
|---|---|---|---|
| *All Patients* | Total 30<br>26 (4-56) | Total 37<br>26 (3-98) | Total 67<br>26 (3-98) |
| *Metastases (M)* | Total 8<br>29 (6-54) | Total 6<br>14 (5-54) | Total 14<br>18 (5-54) |
| *Bulky tumour only (>2cm) (B)* | Total 5<br>20 (7-31) | Total 7<br>20 (3-51) | Total 12<br>20 (3-51) |
| *M and B* | Total 13<br>24 (6-54) | Total 13<br>17 (3-54) | Total 26<br>18 (3-54) |
| *Remaining patients* | Total 17<br>30 (6-57) | Total 24<br>30 (4-98) | Total 41<br>30 (4-98) |

### 4.3.6 Complications and Intubation

Radiotherapy was generally tolerated well. Mild nausea, lethargy, and odynophagia were not uncommon during treatment but as in the pilot study this did not amount to more than a minor irritant for most patients. Three patients did however suffer deterioration following radiotherapy, 2 deteriorated fairly rapidly after treatment and died within a few weeks (see below) and one suffered with pain probably due to oesophagitis which was only partially relieved with acid suppression with omeprazole. It is impossible to be certain if the deterioration was radiotherapy or disease related, indeed 4 patients who did not receive radiotherapy deteriorated over a similar time interval following trial entry.

Patients with squamous cell cancers who received radiotherapy were more likely to develop predominantly fibrous strictures (10/14 v 3/11 who received laser only) and treatment of such strictures resulted in the opening up of fistulae in 2 patients (see below).

In all 25 patients required oesophageal prostheses a median of 13 weeks (range 0-60 weeks) after 'check' endoscopy. Fourteen had received radiotherapy and 11 had not. Twenty four were inserted into patients who were having difficulty managing a semi-solid diet for most of the time. Sixteen of these patients predominantly had troublesome extrinsic strictures and 8 predominant intraluminal tumour which was no longer adequately controlled with laser. Standard Celestin prostheses were used in all but 3 of these patients who received cuffed Wilson Cooke tubes. All three had tight strictures which developed following radiotherapy, 2 developed fistulae (one oesophagobronchial, one oesophagopleural) and one a perforation after dilatation. Both fistulae occurred in elderly female patients with squamous cell cancers, one cervical and one lower thoracic, both died shortly after intubation. Two of these patients including one with a fistula developed the complication within a few weeks of radiotherapy. The other fistula occurred late (20 weeks after radiotherapy). One further perforation occurred after dilatation in an elderly patient with a cardia cancer. She had also undergone radiotherapy over a year before the complication arose and survived a further 16 weeks with a Celestin tube.

The other intubation was performed for uncontrollable bleeding from a cardia cancer in a 75 year old male who had not received radiotherapy. A Wilson Cooke cuffed tube was used to splint the tumour and the life threatening bleeding was arrested. He survived a further 6 months swallowing most solids.

All but 2 of the patients have died at the time of writing. Excluding those with fistulae, none died of aspiration pneumonia, all developed symptoms of progressive cancer such as cancer cachexia and/or the effects of metastatic disease.

### 4.3.7 Patients with bulky Tumours and Metastases

Nineteen patients had bulky tumours at initial endoluminal ultrasound (>2cm wall thickness) and 16 of these had malignant looking nodes, 7 also had known metastases. There was no difference in tumour length in this group compared with the other trial patients (median tumour length 8cm range 5-16cm). Nine were randomised to receive radiotherapy but the 2 patients subsequently deemed unfit who did not receive radiotherapy were in this group so only 7 received radiotherapy. (The patient deemed unfit after randomisation who only had 2 fractions of radiotherapy did not undergo endoluminal ultrasound). Two of the 7 tolerated radiotherapy badly and died within a few weeks. Despite this most patients in this group swallowed well, the median follow up dysphagia grade being 1 and only one patient worse than 2. Those receiving radiotherapy did equally well in palliation of dysphagia. Considering bulky cardia cancers 6 of 11 (55%) could only manage a semi-solid diet or worse despite apparently adequate recanalisation. The difference in swallowing between these patients and the rest of the group is not significant (Wilcoxon Rank sum) but the numbers are small. This may represent a real difference which may be explained by pseudoachalasia (discussed later). The DCI data and weeks of follow up per endoscopy for this group are very similar to that for the group as a whole.

## 4.4 Discussion

Accepting that there is both a benefit for laser in comparison to intubation in terms of quality of swallowing and fewer complications, this study has attempted to address the main problem with laser, that is the necessity for frequent repeated treatments. The results show quite clearly that the combination of laser and palliative external beam radiotherapy goes some way toward this aim. To increase the follow up period from 5 to 9 weeks is a significant improvement. The effect is greater for patients with squamous cell cancers although the difference within this group did not reach statistical significance (probably type 2 error due to small numbers).

The use of the Aloka probe for endoluminal ultrasound confirmed late stage disease in most patients. It is a far cheaper option than the standard Olympus echo-endoscope such as the EU M2 (around £50,000). It need only involve the additional expense of purchasing an oesophageal transducer (around £5,000) if a suitable conventional console is available. The standard probe is 7.5 MHz and the Aloka probe only 5MHz. Image resolution of this lower frequency is less good in the near range and was insufficient to show layers in normal oesophageal wall. It is possible that this problem could be addressed by the addition of a standoff balloon if patients with early oesophageal cancer were to be assessed. Discriminating between normal and diseased oesophagus was however not a problem and views of perioesophageal tissues, nodes and surrounding structures was good. On occasions the finding of a thin oesophageal wall or close opposition of important structures such as trachea or aorta helped direct laser treatment away from such hazards.

The ultrasound strongly suggested malignant lymphadenopathy in 75% of these patients. Three of thirteen patients with nodes > 1cm (23%) in the radiotherapy group showed a partial response (node size reduced by 50% or more). Overall there was no statistically significant change in wall thickness or node size at 'check' endoscopy in either arm of the study. There was however a trend toward a reduction in node size in the radiotherapy group. The measurements of oesophageal wall thickness must be treated with some caution in view of the necessity to perform examinations immediately following laser treatment in many cases. It is disappointing that the effect of external beam radiotherapy on local tumour appears to be so limited

In a previous study from this unit (Loizou 1991) a number of patients did not swallow well despite apparently adequate laser recanalisation. This was ascribed to pseudoachalasia due to patients with bulky cardia tumours. It is interesting that 6 of 11 patients with such tumours (>2cm thick) in the present study swallowed no better than they would have done with a tube. The ultrasound may be useful in identifying these patients who would benefit from early intubation unless swallowing solids after laser. As radiotherapy was poorly tolerated in 2/7 of those with bulky tumours such patients probably should not receive radiotherapy even if laser treatment is pursued. Also in view of the poor survival (median 17 weeks) of those with metastases or bulky tumours who received radiotherapy such patients probably would do better with laser only.

The survival data in this randomised study shows a similar spectrum regardless of treatment arm. If patients with metastases and large tumours are excluded the median survival is identical in both groups. It is worth noting however that 2 patients with adenocarcinomas of the cardia who received radiotherapy survived for long periods (76 and 98 weeks). This prolonged survival is seen as a 'tail' on the survival curve. Both were elderly females and had neither bulky tumours (>2cm thick) nor metastases at presentation, but otherwise had no clear characteristics different from the rest of the group.

It is disappointing that a more definitive difference in survival did not emerge in view of the results in the pilot study. However the main aim of giving radiotherapy in addition to laser was to prolong dysphagia controlled intervals and length of survival is a secondary concern in this group of patients.

Relatively few complications occurred though it is of concern that the major cases were patients undergoing radiotherapy. This may be partly due to the tendency for tight fibrous strictures to develop in patients with squamous cell cancers treated with external beam radiotherapy. It is important to be aware of the potential for this problem as extra care during dilatation may avert it. Intubation was performed late in patients in whom the preferred treatment was unsuccessful and the relative lack of complications for such procedures was encouraging. The only 2 treatment related deaths occurred in patients who had known fistulae following dilatations.

Overall these results imply an average of only one therapeutic endoscopy saved per patient by the use of external beam radiotherapy; however those who live longer may save 2 or more procedures. On the basis of these results it is unlikely that external beam radiotherapy will benefit most patients undergoing palliation for malignant dysphagia. It could however be argued that additional palliative external beam radiotherapy is worthwhile for selected patients who are inoperable and who do not have bulky disease or metastases. In particular those who are relatively fit but may have to travel long distances for each treatment who prefer a longer admission at the start of treatment. Such patients are likely to live long enough to benefit. Perhaps more importantly this study has shown that external beam radiotherapy in addition to laser *is* having a useful effect on the tumour. It may be that this effect can be further improved by addition of local radiotherapy (brachytherapy) in regimes which give higher doses in a smaller number of fractions. These can be administered more rapidly, and without prolonged hospitalisation.

Other endoscopic techniques for relieving swallowing such as alcohol injection or BICAP probe have been shown effective in the palliation of malignant dysphagia (Payne James 1990, Jensen 1988). It is likely that any benefit seen with radiotherapy in combination with laser would be mirrored for such techniques and appropriate studies with these combinations should be encouraged.

# CHAPTER 5

## A QUALITY OF LIFE ANALYSIS IN PATIENTS UNDERGOING LASER OR LASER WITH RADIOTHERAPY FOR MALIGNANT DYSPHAGIA

### 5.1 Aims and rationale

The success or otherwise of cancer treatments is usually measured by assessing tumour response and patient survival rates. Improved swallowing has been generally accepted as an important measure of efficacy of palliation in incurable patients treated for malignant dysphagia. In the preceding chapter we have demonstrated no important difference in tumour response, as measured by node size with endoluminal ultrasound, and no important survival difference between patients receiving additional radiotherapy and those treated with laser only. Swallowing appears to be palliated equally well in those receiving each of the treatment regimes. There is some evidence that patient quality of life is correlated with quality of swallowing (Barr et al 1991, Loizou et al 1992), although the first study found a poorer correlation than the latter. Thus although palliation of dysphagia is important in these patients other factors do effect quality of life. When assessing response to therapy it is desirable that quality of life assessments are made in addition to dysphagia scores. In particular we wanted to assess if additional external beam radiotherapy was having any adverse effect on the patients quality of life. Particular emphasis was placed on quality of life assessments for the period after adequate recanalisation when those randomised to radiotherapy received radiation. The intention was to confirm the subjective impression that the regime of external beam radiotherapy of 30Gy in 10 fractions caused no more than a temporary set back in this patient group.

## 5.2 Methods

### 5.2.1 Prospective evaluation of quality of life

Prospective evaluation was performed using a Quality of Life Index (QLI, Spitzer 1981) and a Linear Analogue Self-Assessment (LASA, Priestman 1976). The assessments were initially performed by myself and subsequently by the research sister (ST) after instruction. The QLI assessment (figure 5.1) includes physical, social and emotional aspects of life and was made following a structured interview. The assessment examined five parameters, activity, daily living, health, support and outlook. Each item is scored between 0 and 2 giving an overall score of 0 to 10. The QLI has been carefully validated (Spitzer 1981) and appears particularly discriminant when used for patients with cancer and other chronic diseases.

The LASA questionnaire has been assessed in detail in patients receiving treatment for advanced breast cancer (Priestman 1976). The technique has been shown to be reliable and there is a high degree of correlation between patients scores obtained with and without a doctor being present. The questionnaire used in this study consisted of 5 visual analogue scales and was completed by the patient after appropriate explanation. Each scale used a 10cm line with a word at each end denoting the poorest (0cm) and the best extremes (10cm). Symptom control and physical well being were examined in detail. Previous versions of this method of assessment have used 10 or even 20 parameters. Those with the larger number of parameters have run into problems with patient compliance (Loizou et al 1992). We therefore concentrated on a smaller number of parameters which were likely to be influenced by radiotherapy treatment (figure 5.2). Both quality of life assessments and assessment of dysphagia grade were performed after initial tumour recanalisation when the patients consented to the trial. An attempt was made to perform subsequent assessments at the 'check' endoscopy and at each hospital visit afterwards. Where possible QLI assessments were also made by telephone in those under follow up who did not require admission, LASA scores which require patients to make a mark on a line were not performed in these circumstances.

## Figure 5.1 (QL Index assessment)

| | | |
|---|---|---|
| ACTIVITY | During the last week the patient | |
| | - has been working or studying full time or nearly to in usual occupation or managing own household, or participating in unpaid or voluntary activities whether retired or not. | 2 |
| | -has been working or studying in usual occupation or managing household or participating in unpaid or voluntary activities, but requiring major assistance or a significant reduction in hours worked or sheltered situation or was on sick leave. | 1 |
| | - has not been working or studying in any capacity and not managing own household. | 0 |
| LIVING | During the last week the patient | |
| | - has been self reliant in eating, washing, toiletting and dressing, using public transport, or driving own car. | 2 |
| | - has been requiring assistance (another person or special equipment) for daily activities and transport but performing light tasks. | 1 |
| | -has not been managing personal care nor light tasks and/or leaving own home or institution at all. | 0 |
| HEALTH | During the last week the patient | |
| | - has been appearing to feel well or reporting feeling great most of the time. | 2 |
| | - has been lacking energy or not feeling entirely 'up to par' for more than occasionally. | 1 |
| | - has been feeling very ill, or lousy, seeming very weak and washed out most of the time or was unconscious. | 0 |
| SUPPORT | During the last week the patient | |
| | - the patient has been having good relationships with others and receiving strong support from at least one family member or friend. | 2 |
| | - support received or perceived has been limited from family and friends and/or by the patient's condition. | 1 |
| | - support from family and friends occurred infrequently or only when absolutely necessary or patient was unconscious. | 0 |
| OUTLOOK | During the last week the patient | |
| | - has usually been appearing calm and positive in outlook, accepting and in control or personal circumstances, including surroundings. | 2 |
| | - has sometimes been troubled because not fully in control of personal circumstances or has been having periods of obvious anxiety or depression. | 1 |
| | - has been seriously confused or very frightened or consistently anxious or depressed or unconscious. | 0 |

**Figure 5.2**

*PLEASE MARK EACH LINE ACCORDING TO HOW YOU FEEL.*

PAIN ON SWALLOWING

SEVERE NONE

TIREDNESS

TIRED NOT TIRED

APPETITE

VERY POOR VERY GOOD

NAUSEA OR VOMITING

CONSTANT NONE

HOW DO YOU FEEL

VERY UNWELL VERY WELL

### 5.2.2 Retrospective evaluations

Patients entered into this study were seen on average five or six times during the course of their illness and spent enough time in hospital for us to get to know them. On the basis of data collected during these hospital visits and from telephone conversations with the research sister patients were categorised into one of 4 groups. This 'Subjective assessment' of their overall quality of life includes a crude assessment of symptoms and activity and is later referred to as the subjective quality of life assessment. These are as follows.

1. Disease and/or treatment have either no or only a minimal effect on quality of life which amount to no more than minimal symptoms or minimal effect on the patients daily routine.

2. Disease and/or treatment result in a definite reduction of quality of life for most of the patients remaining life. The impairment in quality of life is however mild and the patient is not perpetually troubled with symptoms and is able to look after him/herself for most of remaining life.

3.Disease and/or treatment result in a major deterioration in quality of life. The patient suffers with symptoms much of the time or has difficulty performing activities of daily living without assistance. The treatment however appears to be of some benefit and the patient still appears to have a worthwhile existence for most of remaining life.

4. Disease and/or treatment result in a very poor quality of life. The patient suffers with severe symptoms most of the time, and/or needs constant nursing support. Treatment has little or no benefit and the patient suffers a relentless downhill course such that it appears that the patient has gained nothing from laser/radiotherapy.

### 5.3 Statistical analysis

The degree and significance of correlation between various indices were calculated using the Spearman rank correlation method. Differences between paired data were tested using the Wilcoxon signed rank test for non-parametric data. The Mann-Whitney U test was used to compare unpaired groups.

### 5.4 Results

The raw data giving results of quality of life assessments at each stage are given in appendix 4.

#### 5.4.1 The effect of radiotherapy on quality of life measures

Most of the assessments were performed around the time of treatment with external beam radiotherapy (or equivalent in those randomised to laser only) as an important reason for performing these assessments was to document any radiotherapy effect on quality of life.

QLI 1 and LASA 1 were performed at randomisation ( after laser recanalisation)
QL1 2 and LASA 2 were performed after one week of radiotherapy (these assessments were only made in those receiving radiotherapy)
QLI CK and LASA CK were performed in patients in both trial arms at the 'check' endoscopy (five weeks after randomisation or 3 weeks after completion of radiotherapy in those so treated)

The numerical data for quality of life measures at each stage is given in tables 5.1 and 5.2.

Table 5.1

QL index data

| Parameter | No | Mean | Median |
|---|---|---|---|
| QLI 1 All | 37 | 8.1 | 8.0 |
| QLI 1 No RT | 17 | 8.4 | 9.0 |
| QLI 1 RT* | 20 | 7.8 | 8.0 |
| QLI 2 RT* | 21 | 7.1 | 7.0 |
| QLI CK All | 47 | 7.9 | 8.0 |
| QLI Ck RT | 26 | 7.7 | 8.0 |
| QLI Ck No RT | 21 | 8.2 | 9.0 |

The Mann-Whitney U test was applied to campare sets of data and no significant differences were observed. The Wilcoxon signed rank test was used to compare matched pairs the only significant difference is marked * and p =0.014 for 13 paired observations

Table 5.2

LASA Data

| Parameter | No | Mean | Median |
|---|---|---|---|
| LASA 1 All | 34 | 38.7 | 40 |
| LASA 1 No RT | 16 | 40.0 | 41 |
| LASA 1 RT | 18 | 37.6 | 40 |
| LASA 2 RT | 21 | 35.4 | 36 |
| LASA CK All | 40 | 37.6 | 39 |
| LASA Ck RT | 23 | 35.3 | 36 |
| LASA Ck No RT | 17 | 40.7 | 42 |

The Mann-Whitney U test was applied to campare sets of data and no significant differences were observed. The Wilcoxon signed rank test was used to compare matched pairs and again there were no significant differences.

Both the QLI index and the LASA measures register a fall during radiotherapy treatment. The magnitude of this fall is however small. The median QLI falls from 8.0 to 7.0 and the LASA from 40 to 36. The reduction in QLI score is statistically significant but the reduction in LASA score is not (Wilcoxon signed rank test for matched pairs). Assessing all the data with the Mann-Whitney U test revealed no differences between any of the groups.

Subjective quality of life assessments were comparable in both groups. The median score was 2. The mean grade was slightly lower (ie better swallowing) in the laser only group 1.9 v 2.3 (possibly reflecting slightly better QLI and LASA scores in the laser only group after initial recanalisation and before radiotherapy). The difference was not significant.

### 5.4.2 Correlation between quality of life measures used

Correlation coefficients between the quality of life measures used are given in table 5.3 and is demonstrated graphically in figure 5.3. The correlation between all 3 measures is strong and highly significant. The subjective assessments were only made once. We chose to correlate these with the data at 'check' endoscopy. These were performed 5 weeks after randomisation and we deemed them the most likely to be representative of the overall result of treatment. Also more data were available at that time.

It is interesting to note that the correlation between our subjective assessment and the LASA and QLI indices at the 'check' endoscopy appears equally strong as between the LASA and QLI indices themselves.

## Table 5.3

### Correlation between quality of life measures

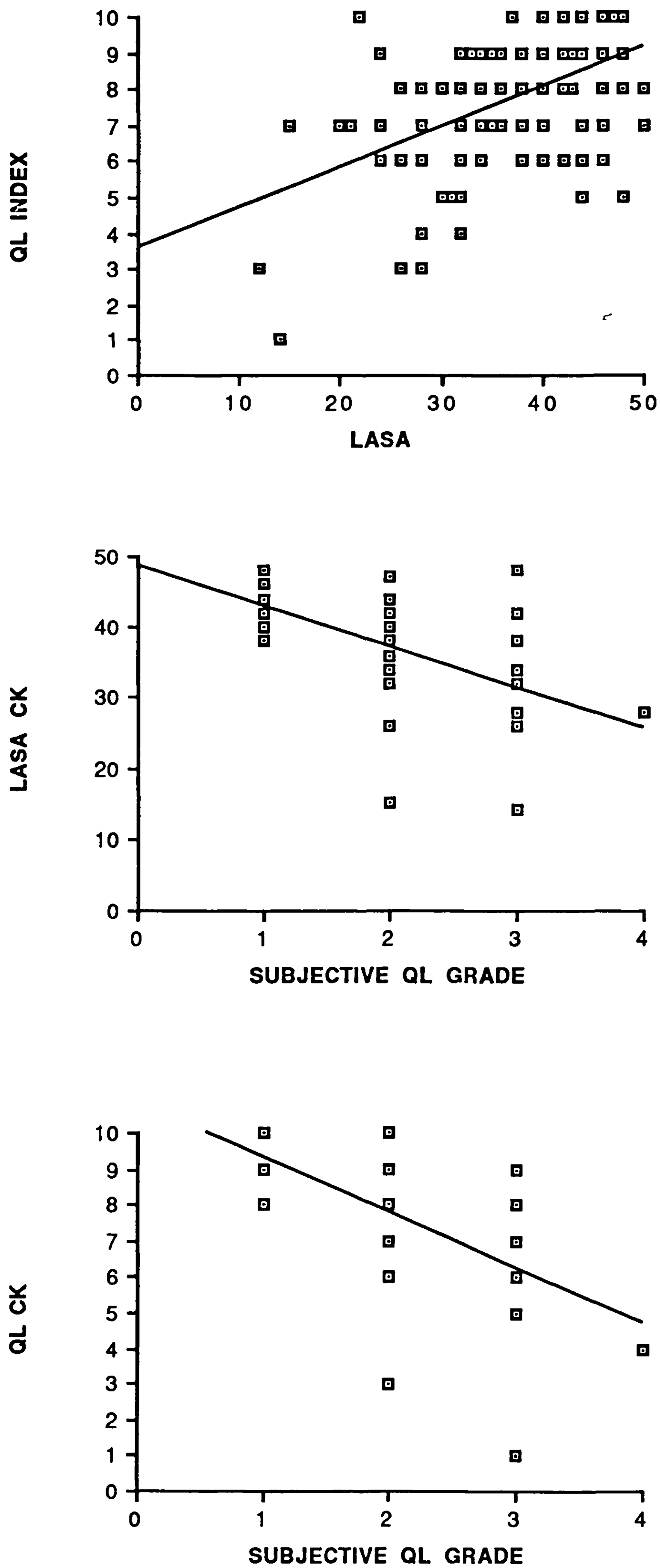
| Parameter | No of paired observations | Correlation coefficient | Significance |
|---|---|---|---|
| QLI versus LASA | 148 | O.506 | <0.001 |
| SUB QL versus QLI CK | 47 | -0.691 | <0.001 |
| SUB QL versus LASA CK | 40 | -0.593 | <0.001 |

SUB QL = Subjective quality of life assessment

QLI = QL index

LASA = Linear analogue self assessment

Figure 5.3



QL INDEX
10
9
8
7
6
5
4
3
2
1
0
0
10
20
30
40
50
LASA
LASA CK
50
40
30
20
10
0
0
1
2
3
4
SUBJECTIVE QL GRADE
QL CK
10
9
8
7
6
5
4
3
2
1
0
0
1
2
3
4
SUBJECTIVE QL GRADE

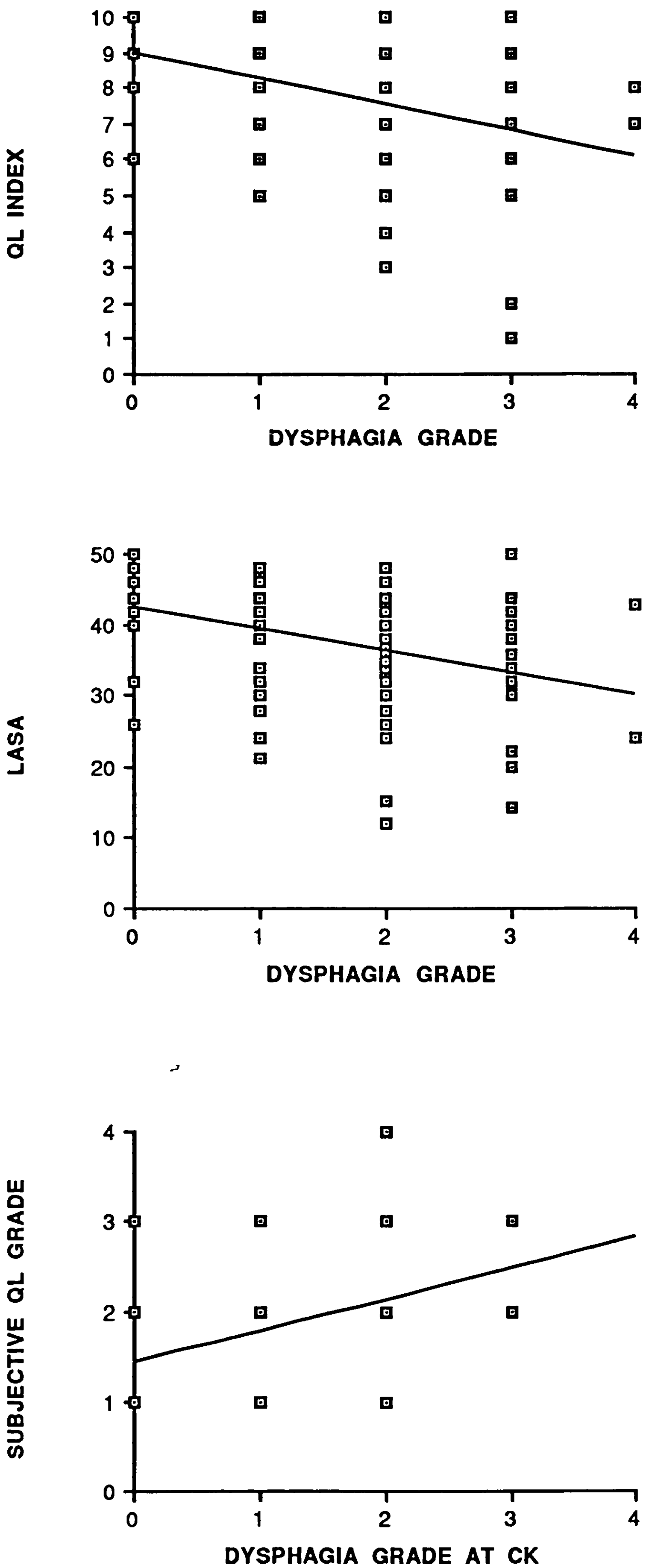
### 5.4.3 Correlation between quality of life measures and dysphagia grade

Correlation coefficients between paired dysphagia grades and each quality of life score are given in table 5.4 and shown graphically in figure 5.4. Paired results are available on 64 patients in all and the number of observations is given in the table. There is a moderate correlation between the dysphagia grades recorded and the quality of life assessments which is statistically significant. The square of the correlation coefficient (r squared) gives the proportion of the variability in x which can be accounted for by y. Thus only 0.18 (18%) of the variability in the QL index can be accounted for by the dysphagia grade.

**Table 5.4**

| Parameter | No of paired observations | Correlation coefficient | Significance |
|---|---|---|---|
| QL index versus DG | 164 | -0.374 | <0.001 |
| LASA versus DG | 148 | -0.363 | <0.001 |
| SUB QL versus DG CK | 47 | 0.445 | 0.002 |

**Figure 5.4**



QL INDEX
10
9
8
7
6
5
4
3
2
1
0
0
1
2
3
4
DYSPHAGIA GRADE
LASA
50
40
30
20
10
0
0
1
2
3
4
DYSPHAGIA GRADE
SUBJECTIVE QL GRADE
4
3
2
1
0
0
1
2
3
4
DYSPHAGIA GRADE AT CK

5.4.4 <u>Change in quality of life with time</u>

Further quality of life assessments were made where possible as follows. Most of these assessments were made while patients were readmitted for further procedures and not on patients admitted for terminal care which was normally given in referring hospitals.

| | |
|---|---|
| QLI 4 and LASA 4 | 1-3 months after 'check' endoscopy |
| QLI 5 and LASA 5 | 4-6 months after 'check' endoscopy |
| QLI 6 and LASA 6 | 7-9 moths after 'check' endoscopy |

Data on these measures is given in table 5.5. There is no significant reduction in scores with time. The scores for patients receiving radiotherapy remain very slightly lower than those for the laser only treated patients but the differences are not significant.

**Table 5.5**

| Parameter | No | Mean | Median |
|---|---|---|---|
| QLI 4 | 32 | 7.7 | 8.0 |
| LASA 4 | 26 | 38.2 | 41 |
| QLI 5 | 19 | 7.8 | 8.0 |
| LASA 5 | 19 | 36.5 | 38 |
| QLI 6 | 10 | 8.0 | 8.0 |
| LASA 6 | 10 | 35.4 | 39 |

The Mann-Whitney U test was applied to campare sets of data and no significant differences were observed. The Wilcoxon signed rank test was used to compare matched pairs, no significant difreences were found.

It is interesting to note that despite the consistency in quality of life assessments there is a progressive reduction in dysphagia grade with time as follows.

| | Mean | Median |
|---|---|---|
| DG CK* | 1.4 | 1 |
| DG 4 | 1.7 | 2 |
| DG 5* | 2.0 | 2 |
| DG 6 | 2.1 | 2 |

* Wilcoxon signed rank 13 matched pairs $p<0.01$.

### 5.5 Discussion

It has previously been shown that quality of life improves quite dramatically with initial laser recanalisation in patients treated for malignant dysphagia (Loizou 1992, Barr 1991). In this study we did not assess patients prior to recanalisation but concentrated on assessments during and after radiotherapy treatment.

Overall quality of life assessments were performed on only about half of the occasions initially intended. This compares quite favourably with data from the previous studies mentioned. This unwillingness may be at least partly a psychological defence against the inevitable progressive deterioration in these patients. Many patients were reluctant to participate in the assessments and comprehension difficulties accounted for a slightly lower participation in the LASA tests.

The most important reason for obtaining quality of life data in this study was to confirm the subjective findings of the pilot study that the 30Gy in 10 fractions course of radiotherapy was well tolerated. We have shown a small temporary fall in score of both quality of life measures used during radiotherapy treatment. The drop in the QL index reaches statistical significance. Both measures rise again 3 weeks after radiotherapy and at no time afterwards is there any significant difference between results recorded at different times. There are also no significant differences in the results of all 3 quality of life measures employed between those receiving radiotherapy and those treated with laser only. These findings confirm our subjective impression that the radiotherapy regime employed was well tolerated. It is however important to note that data is only available on a proportion of the patients and it is possible that we did not have enough data to detect a difference (type 2 error or false negative finding).

It is reassuring that we obtained such a good correlation between each of the quality of life measures. In particular we feel this strengthens the validity of a very simple approach such as our subjective assessments. These assessments had the advantage that all patients could be graded as they were performed retrospectively solely by the physician and no patient participation was required. For future studies such an assessment on a prospective basis is attractive. We probably should not be surprised that the LASA scores do not correlate quite so well with the others as we specifically designed this to document symptoms likely to be worsened with radiotherapy .

The correlation between quality of life measures and dysphagia grade was significant but fairly loose. Clearly dysphagia is important to quality of life in these patients but only 18 % of the variation in QL index could be accounted for by the dysphagia grade. Thus other factors are also important. It is likely that these factors are related to the growth of the tumour itself and thus there is no easy remedy. Therapeutic interventions aimed at achieving the best possible swallowing are therefore likely to improve quality of life.

The later assessments however show a statistically significant fall in dysphagia grade while quality of life scores are almost static. Most patients are still however swallowing semi-solids at this time. It may be that the supportive role of hospitalisation at this time is maintaining quality of life despite the worsening dysphagia.

The reliance on dysphagia grade alone to measure success in palliation of malignant dysphagia does not give the whole picture. These results however demonstrated a fair degree of correlation between quality of life and quality of swallowing and have demonstrated that the radiotherapy given caused no more than a temporary dip in quality of life scores.

# CHAPTER 6

## AN ECONOMIC EVALUATION OF THE USE OF EXTERNAL BEAM RADIOTHERAPY IN ADDITION TO LASER IN PALLIATION OF MALIGNANT DYSPHAGIA

### 6.1 Background and Rationale

There is increasing need for health care purchasers to consider the relative cost implications of alternative health care interventions as well as their outcomes. To date there has been only one study performed on the cost of primary treatments for palliation of patients with malignant dysphagia (Sculpher et al 1994). This study looked in detail at the relative costs of laser and conventional tubes, it was a joint effort between the Health economics research group at Brunel University and our unit at UCH. A cost model was defined describing key clinical pathways along which a patient undergoing palliation may pass. The probability of an individual passing down any given pathway was calculated using five published comparisons of laser and tube in addition to UCH data. The health service resource use associated with each pathway was calculated using data from the laser v tube study (Loizou 1991) and from patients treated with laser only in the study described in chapter 4 (laser v laser and radiotherapy). This approach allowed us to cost the other studies using data for resource use at UCH. The analysis demonstrated that laser costs between £153 and £710 more than tube for any individual. This represents a small percentage of the total cost of treatment during the mean survival time of 5-6 months. As laser does offer better swallowing it is likely that this extra cost results in a significantly better health related quality of life and that the small additional cost is money well spent. However further research is required to formally assess if the improvement in quality of life is sufficient for laser alone as primary treatment to be cost effective in comparison to intubation.

The objective of the present analysis was to estimate the additional cost (or saving) resulting from the use of external beam radiotherapy at a dose of 30Gy in 10 fractions in addition to the Nd YAG laser as primary palliation for malignant dysphagia. Clearly there would be some additional cost of performing radiotherapy as this involves an additional treatment which often required admission. However we hoped that this cost may be offset by a saving on the total number of therapeutic endoscopies required which also frequently requires in-patient treatment resulting in further hospitalisation costs. If additional treatment with external beam radiotherapy allowed a modest reduction in hospitalisation for therapeutic procedures it could have resulted in an overall cost saving. The costing exercise undertaken was not intended to be a comprehensive costing of all health care resources expended in these patients. It was designed to concentrate on the difference in cost between patients treated with laser only and those receiving additional external beam radiotherapy.

## 6.2 Methods

The analysis was performed using data from the randomised study of laser versus laser and external beam radiotherapy (Chapter 4). The cost of the major health service resources used by patients undergoing the two forms of palliation over their remaining lifetimes was assessed. It is assumed that patients survive, on average, the same length of time whatever their palliative therapy; an assumption which is supported by the survival data from the study. The general approach of the analysis was to cost resources on the basis of unit cost data taken from relevant suppliers or from UCH financial records. Many of these costings had been obtained for the laser versus tube economic evaluation. Assessment of the cost of radiotherapy was obtained directly from the appropriate department. The only other cost not covered in the prior study was the cost of the cuffed Wilson Cooke tubes. The advantage of costing a randomised study such as this is that the cost of complications of treatment is covered within the cost of treatment for individual patients. The cost of additional treatment of the few patients in the radiotherapy group who suffered perforations or fistulae is thus inherent in the overall costings. The more elaborate approach of constructing a cost model employed in the study comparing laser and tube was not required. There is also very little data on radiotherapy/laser treatment combinations to which costings can be extrapolated.

### 6.2.1 Assessing resource use

Four categories of resource use were identified.

#### 6.2.1.1 Diagnostic resource use

When patients present with dysphagia they undergo a clinical assessment and a course of staging investigations is often required before a decision is made that palliation is the primary treatment aim. The costs of this initial assessment and subsequent blood tests performed during hospitalisation are assumed to be equal in both groups and are not included in this analysis.

#### 6.2.1.2 Endoscopic procedures

A range of procedures are performed in these patients depending on the clinical need. These comprise a diagnostic procedure, which is sometimes all that is required at the check endoscopy, a dilatation alone, laser alone, dilatation+laser, dilatation+intubation and occasionally dilatation+laser+intubation. The cost of in-patient stay required for these procedures has to be added to the actual procedure cost.

#### 6.2.1.3 External beam radiotherapy

The cost of the two week radiotherapy regime is the third resource use category. Again the cost of hospitalisation in those patients admitted has to be included.

#### 6.2.1.4 Follow up and terminal/supportive care

Our practice is to admit patients directly when they have recurrent dysphagia and thus out patient follow up is almost never undertaken. In any case such costs would not be expected to vary between arms of the trial and they have not been included. In addition to the hospital costs of palliative therapy, many patients require further health care support in the community, especially in the terminal stage of their illness. In practice this support involves a mix of care from friends and relatives, GP's, district nurses, MacMillan nurses and hospice care. Limited data are available of the mix of this care. The important issue is whether there is any difference between those undergoing laser or laser and radiotherapy in terms of this support. For the purposes of this study we assume that, on average, these costs are equal in both groups.

### 6.2.2 Valuing resource use

Resource use is valued using a set of unit costs based on supplier prices or derived from the financial accounts of UCH. All unit costs relate to the 1991-2 financial year. The unit costs of endoscopic procedures includes the costs of staff, consumables such as gloves and tubes, drugs including sedation and reverse sedation and an allocation of hospital overheads. The cost of equipment is also included. The cost of the laser and endoscopes has been amortized to an equivalent annual cost using a 6% discount rate and estimates of expected useful life and annual utilisation. For the laser an annual utilisation of 620 patient-treatment sessions has been used, based on UCH data. The expected duration of endoscopic procedures has been estimated using clinical judgement. Details of important costings are shown in tables 6.1-6.3.

## Table 6.1

Cost data 1

| ITEM OF RESOURCE USE | RELEVANT UNIT | UNIT COST | SOURCE OF DATA | NOTES |
|---|---|---|---|---|
| Celestin dilator | Capital cost | £130 + VAT | Medoc Ltd | Annual equivalent cost calculated assuming a 10 year useful life, 6% discount rate and a base-case annual utilisation of 1500. |
| Tube introducer kit | Capital cost | £133.33 + VAT (average of one in a set) | UCH | Annual equivalent cost calculated assuming a 10 year useful life, 6% discount rate and a base-case annual utilisation of 30). |
| **Consumables** | | | | |
| Gloves | Per pair | £0.70 | UCH | |
| Celestin tube | Per tube | £27.50 + VAT | Medoc Ltd | |
| Cuffed tube | Per tube | £158.60 + VAT | Wilson Cook Ltd | |
| **Drugs** | | | | |
| *Sedation* | | | | |
| Diazemuls | Per patient | £3.23 + 33% dispensing fee | BNF (1991) | |

**Table 6.2**

Cost data 2

| ITEM OF RESOURCE USE | RELEVANT UNIT | UNIT COST | SOURCE OF DATA | NOTES |
|---|---|---|---|---|
| *Endoscopes* | | | | |
| Olympus XQ20 gastroscope | Capital cost | £11,225 + VAT | Keymed Ltd | Annual maintenance cost of £938 + VAT added. Annual equivalent cost calculated assuming a 5 year useful life, 6% discount rate and a base-case annual utilisation of 1760. |
| Olympus IT20 gastroscope | Capital cost | £11,875 + VAT | Keymed Ltd | Annual maintenance cost of £938 + VAT added. Annual equivalent cost calculated assuming a 5 year useful life, 6% discount rate and a base-case annual utilisation of 454. |
| *Other equipment* | | | | |
| Laser fibres | Capital cost | £48.50 + VAT | Surgilase Ltd | Assumed 1 per patient (no matter how many laser procedures). |
| Guidewire | Capital cost | £108 + VAT (pack of 5) | Keymed Ltd | Assumed 1 used for every 10 procedures. |

## Table 6.3

Cost data 3

| ITEM OF RESOURCE USE | RELEVANT UNIT | UNIT COST | SOURCE OF DATA | NOTES |
|---|---|---|---|---|
| **Staff** | | | | |
| *Nursing* | | | | |
| Sister (Grade G) | Annual salary | £16,525 } | Bett (1991) | 11% employers' costs added, mid-range salaries used. Hourly cost based on a 47 week year and 37.5 hour week. |
| Nurse (Grade F) | Annual salary | £14,720 } | | |
| Nurse (Grade D) | Annual salary | £10,950 } | | |
| *Medical* | | | | |
| Consultant | Annual salary | £41,160 | Holdsworth (1991) | 11% employers' costs added, mid-range salary used. Hourly cost based on 45 week year and 40 hour week. |
| **Equipment** | | | | |
| *Lasers* | | | | |
| Nd:YAG | Capital cost | £45,000 + VAT | MBB Medical | Annual maintenance cost of £1500 + VAT added. Annual equivalent cost calculated assuming 10 year useful life, 6% discount rate and a base-case annual utilisation of 620. |

## 6.3 Results

The unit costs for each type of endoscopic procedure are detailed in table 6.4. Other key unit costs include the hotel cost of a night in hospital at £83 (based on UCH data) and a cost of £158 for a cuffed Wilson Cooke tube. In addition to the costs shown a further cost of £57 was added for each laser fibre used on the assumption that each fibre lasts for anything up to 3 laser procedures. The actual costs for each patient in the trial are given in appendix 5. This data is pooled in table 6.5 to show mean costs for each arm of the trial with confidence intervals.

**Table 6.4 Unit costs of endoscopic procedures**

| Endoscopic | Staff | Consumables | Equipment | Drugs | Ba Swallow | Overheads | Total cost in pounds |
|---|---|---|---|---|---|---|---|
| Laser | 56 | 1 | 28 | 13 | - | 18 | 116* |
| Dilatation | 25 | 1 | 6 | 13 | - | 18 | 63 |
| Diagnostic only | 19 | 1 | 3 | 13 | - | 18 | 54 |
| Dilatation+Laser | 75 | 1 | 34 | 13 | - | 18 | 141* |
| Dilatation+Intubation | 75 | 33** | 6 | 13 | 69 | 18 | 214 |
| Dilatation+Laser+Intubation | 93 | 33** | 34 | 13 | 69 | 18 | 260* |

* Laser fibre (cost £57) assumed to last up to 3 procedures. Cost added per patient depending on procedure number

** Includes cost of Celestin tube

**Table 6.5**

**costs of laser v laser + 30Gy DXRT**

| | **Range** | **Mean** | **Median** |
|---|---|---|---|
| **Laser only** | £227-3492 | £1750 | £1769 |
| **Laser+DXRT** | £697-5313 | £2874 | £2606 |

Extra cost of DXRT = £1124 (95% Confidence Intervals £569-£1679)

## 6.4 Discussion

### 6.4.1 Differential cost

The analysis described in this chapter indicates that, over the mean lifespan of 5-6 months that patients with malignant dysphagia are likely to live, palliation of their symptoms with Nd:YAG laser ablation alone cost on average £1,124 less than palliation with laser and external beam radiotherapy. The extra cost of external beam radiotherapy is due to a mean extra hospital stay of 5 nights (£400) and the cost of radiotherapy itself (£830). There is a small cost saving (mean £106) on endoscopic procedures. This data is, of course, based on UCH data and a number of parameters may vary between centres.

Many centres may be able to perform external beam radiotherapy as an outpatient which may significantly reduce the cost of this treatment. If all radiotherapy was done as an out patient the number of nights in hospital would actually be 2 fewer for the radiotherapy group as they require fewer follow up endoscopic procedures. The duration of hospitalisation itself becomes more important as the cost of in patient care rises. The figure supplied to us (£83) is rather low. Most hospitals would now quote figures of £200-250. Using our data this increases the mean cost of radiotherapy treatment by £600-£850. However if all external beam radiotherapy was performed as an out patient the cost in those receiving that treatment would be only around £400 more.

The cost of day-case Brachytherapy is £380. If this treatment was equally effective as external beam radiotherapy in reducing the necessity for follow up procedures there would be no additional cost. Provisional results from our unit indicate that there may be a greater benefit in patients treated in this way resulting in a small cost saving over laser only treatment (Spencer 1994).

### 6.4.2 Cost-effectiveness

The results of this analysis indicate that the Nd YAG laser DXRT combination is more expensive than laser alone. It does not automatically follow that the laser only treatment is more cost effective. This depends crucially on the health outcomes generated by the two therapies. We have already demonstrated no important difference in survival. The other important measure is health related quality of life. This was assessed with the QL-index and LASA tests used in chapter 5 and overall no important differences emerged. It is possible that differences in the quality of life data were missed due to small numbers (type 2 error) however it seems unlikely that the general use of external beam radiotherapy in addition to laser enhances quality of life. Of course this is a generalisation and as we suggested previously there may be certain patients with less extensive tumours who benefit more and thus additional external beam radiotherapy may be appropriate for them.

In order to formally estimate the relative cost effectiveness of two therapies it is necessary to assess the outcome of each therapy on a scale of 0 to 1 (Torrance 1986). These values can then be used to estimate the quality of life years (QALY's) generated by the two therapies (Loomes 1989). If additional radiotherapy is to prove cost effective it has to generate sufficiently more QALY's than laser alone to justify its additional cost. A recent Canadian paper has suggested that if a new intervention can generate more QALY's than conventional therapy at an incremental cost of less than $20,000 (£10,500) it is cost effective and justifies adoption (Laupacis 1992). If we were to apply that threshold to this study additional radiotherapy would have to be valued at least 28% more highly by patients on the 0 to 1 scale. On the basis of the quality of life data we obtained this threshold would not be reached.

# CHAPTER 7

## RADIATION ENHANCEMENT OF LASER PALLIATION FOR ADVANCED RECTAL AND RECTOSIGMOID CANCER : A PILOT STUDY

### 7.1 Background

Unfortunately many patients present with tumours too extensive to resect or are unfit for such surgery. The proportion of patients in this group varies between studies but is over 10% A further group with anastomotic recurrences are often unsuitable for further surgery. A full discussion of the morbidity and mortality of palliative resection can be found in chapter 2. Large studies report serious morbidity of up to 30% (Goligher 1984, Lewis 1988). A further problem is that survival following palliative surgery is limited; one study (Hohenburger 1986) found a median survival of only 8 and 14-16 months in such patients with and without liver metastases. A recent review (Alexander-Williams 1990) advises that surgeons should treat surgically incurable patients with local methods only which are both cost effective and carry a low morbidity and mortality. Nd YAG laser treatment for inoperable rectal and rectosigmoid cancer offers good palliation. Troublesome symptoms such as bleeding, discharge, tenesmus and constipation (due to partial obstruction) can be controlled in most patients with minimal morbidity. Repeat sessions every 4-6 weeks are required for good symptomatic control. This is not surprising as the Nd YAG laser is only capable of safely treating intraluminal tumour. Radiotherapy however has the potential for treating the entire tumour and local regional draining sites and as with oesophageal tumours should be complimentary (Tobias 1991). It has an established record in the treatment of rectal cancer and is commonly used as adjuvant therapy post operatively for Dukes B and C cancers. The risk of local recurrence in this setting is reduced and a randomised MRC trial looking at survival is presently in progress (AXIS trial). The first major series of patients treated by radiotherapy alone for rectal cancer was published in

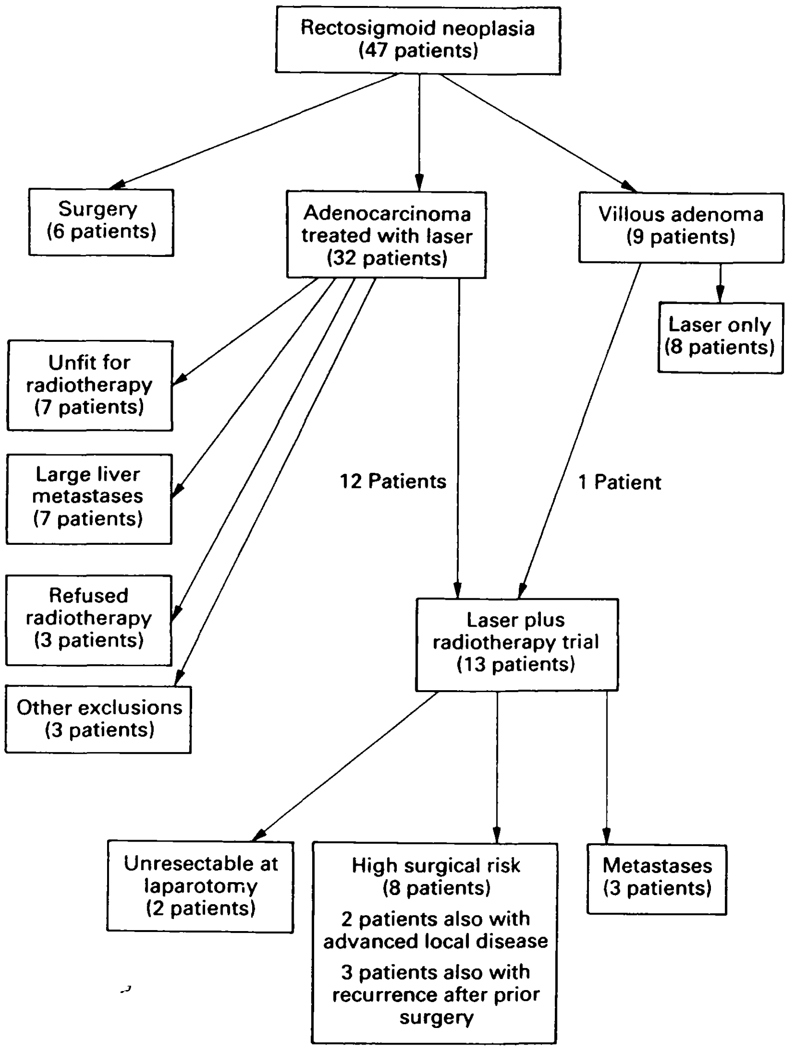
1956 (Williams). Symptomatic palliation was achieved in most patients but complications were common. Half the patients required colostomies either due to obstructive symptoms prior to radiotherapy or from radiation induced fibrosis. Since that time there have been several studies using more modern radiotherapy techniques and fractionation to minimise complications and maximise symptom control for advanced cancers. These are discussed in more detail in chapter 2. Although symptoms can be controlled in the majority of patients it takes several weeks for maximal effect and prolonged relief requires higher radiation doses regimes. These carry a higher risk of complications such as radiation swelling or fibrosis, which can in turn lead to obstruction and may even require permanent colostomy. By treating with laser and radiotherapy we aimed to achieve the benefits of both while minimising complications. Laser can offer rapid relief of rectal discharge and obstructive symptoms, which should reduce the risk of obstruction from radiation induced swelling or fibrosis. Radiotherapy often relieves pain which is untreatable with laser, and may give better long term control so that repeat laser procedures are required less frequently. Two studies using combined laser and radiotherapy in oesophageal cancer (Chapters 3 and 4) produced promising results. Here we present the results of a prospective pilot study of combination laser and radiotherapy for palliation of advanced rectal cancer.

## 7.2 Patients and methods

### 7.2.1 Patient selection

Forty seven patients with rectal and rectosigmoid tumours referred for laser treatment during an 18 month period between February 1990 and August 1991 were considered for inclusion in this study. All patients had been considered unsuitable for surgery either due to incurable disease (documented distal metastases or advanced locoregional disease), or high surgical risk such as advanced age or severe cardiorespiratory disease; 80% were tertiary referrals. The flow diagram (Figure 7.1) gives a detailed breakdown of patients included and excluded.

**Figure 7.1 Flow diagram of all referrals with rectosigmoid neoplasia**



After further assessment 6 patients were considered to be inappropriate referrals and were returned for surgery, {2 total obstruction, 1 tumour invading anus, 3 fit for surgery and resectable by anterior resection}. A further 8 patients with villous adenomas but no evidence of malignant change, were deemed unsuitable for the study and were treated with laser only.

Of 32 patients with proven cancer treated with laser 12 (38%) were entered into the study. Reasons for exclusion in this group were large liver metastases (7), carcinoma but considered unfit for radiotherapy (7, inc 2 sigmoid lesions), radiotherapy refusal (3), previous radiotherapy (1), rectovaginal fistula (1), unable to pass stricture {thus radiotherapy likely to induce obstruction} (1).

Thirteen patients (7 men, 6 women) age 65-91 (median 81) were considered suitable for radiotherapy by Dr Tobias, the radiotherapist, after a good initial laser result. Predominant symptoms were bloody discharge in 8 patients, 2 of whom also had obstructive symptoms and diarrhoea in 5, 2 of whom also had tenesmus and one fecal incontinence (see appendix 6). Eleven of these patients had rectal/rectosigmoid adenocarcinoma (including one with cancerous change in a villous adenoma), one had direct rectal invasion from cervical cancer and one an extensive villous adenoma (with no documented focus of adenocarcinoma). Eleven were considered unfit for surgery, including 3 with metastases and 3 recurrences following surgery, 2 of whom had rectal stump recurrences following A-P resections. The other 2 tumours were unresectable at laparotomy. The tumour length was 2-14 cm (median 5cm) and the lower margin of the tumour was at 0-14 cm (median 6 cm) from the anal verge. At least six patients with lesions less than 7cm from the anal margin would have required permanent colostomy if palliative resection had been carried out. Eight patients had circumferential lesions (C3) and 5 had 1/3-2/3 circumferential lesions (C2).

### 7.2.2 Techniques

Endoscopic and laser techniques have been covered in detail in chapter 1. All patients were irradiated using supervoltage teletherapy (cobalt 60). The target volume was generally determined by CT scanning and, if necessary, barium studies and treatment was delivered using anterior and posterior opposed fields in all cases. Dosage was decided on the basis of the patients general condition, more radical regimes being offered to the younger fitter patients. Ten received a dose of 30Gy in 10 fractions and one patient was re-treated with the same dose when rectal discharge recurred after nine months. One patient received 40Gy in 20 fractions and a further two patients received doses of 50 and 55 Gy in 20 fractions. All treatments were given on consecutive days (weekends excepted).

### 7.2.3 Patient follow up and evaluation

Ten patients underwent check sigmoidoscopy 3-6 weeks after radiotherapy was completed. Response to radiotherapy was assessed, and further laser performed if viable tumour was identified. Three patients did not return for a check as they were asymptomatic. Patients with little or no residual intraluminal tumour and a good lumen (implying minimal risk of obstruction) were not given a further follow up appointment. Those with tumour regrowth requiring laser energy of around 5,000J or more and/or those with a stricture which would not immediately allow scope passage were given a follow up appointment for 4-6 weeks for repeat laser endoscopy. This was essential as if there is a possibility of obstruction developing it is inappropriate in this patient group to wait for symptoms to develop. Inevitably, follow up appointments were given to some extent on a subjective basis according to the laser endoscopists prior experience. As all these procedures were carried out by 2 endoscopists (Myself and Professor Bown) we do not consider that this lead to significant bias. All patients were subsequently contacted monthly by the research nurse to document progress and assess the necessity for further treatment. Patients were evaluated according to endoscopic result, early and late functional success, necessity for repeat endoscopic treatment and dose rate of laser energy required to control intraluminal tumour (averaged laser energy per month).

### 7.2.4 Statistical methods

Paired data for laser energy per month required and for frequency of endoscopic treatment for before and after radiotherapy were analysed using the Wilcoxon signed rank test for both parameters.

## 7.3 Results

A summary of endoscopic and 'functional success' data is given table 7.1. Figures 7.2 and 7.3 show symptomatic response of bleeding and diarrhoea in detail. The predominant symptom for each individual has been assessed. The treatment interval data is given in table 7.2.

**Table 7.1 Endoscopic and symptom results**

| | C2 tumour (5) | C3 tumour (8) | All tumours |
|---|---|---|---|
| Endoscopic result at 'check' | 3 Good<br>2 no Ck | 5 Good<br>2 Strictures<br>1 no Ck* | 8 Good<br>2 Strictures<br>3 no Ck |
| Early functional success | 5/5 | 8/8 | 13/13 |
| Late functional success | 5/5 (100%) | 6/8 (75%) | 11/13 (85%) |

* This patient benefited from late fuctional success

**Figure 7.2 Results of laser followed by radiotherapy for patients with rectal bleeding**

| | Before laser | After laser | After radiotherapy |
|---|---|---|---|
| **Moderate** (fresh frequent loss 5-10/day) | 5 | 0 | 0 |
| **Mild** (intermittent small loss 2-5 / day) | 3 | 3 | 2 |
| **None** | 0 | 5 | 6 |

**Figure 7.3 Results of laser followed by radiotherapy for patients with diarrhoea**

| | Before laser | After laser | After radiotherapy |
|---|---|---|---|
| **Incapacitating** (> 1 per hour) | 2 | 0 | 0 |
| **Severe** (10-20 per day) | 1 | 1 | 1 |
| **Moderate** (3-10 per day) | 2 | 2 | 1 |
| **Comfortable** (near normal) | 0 | 2 | 3 |

**Table 7.2 Treatment interval data in weeks before and after radiotherapy**

| | Treatment intervals in weeks (C2 tumours) | Treatment intervals in weeks (C3 tumours) | Treatment intervals in weeks (all tumours) |
|---|---|---|---|
| Pre DXRT (7 patients followed for > 3 months prior to DXRT) | 7-12 (median 8) | 3-4 (median 3) | 3-12* (median 4) |
| Post DXRT (7 patients as above) | 14-112 (median 42) | 6-53 (median 12) | 6-112* (median 14) |
| Post DXRT procedure interval (all 13 patients) | 9-112 (median 42) | 6-53 (median 9) | 6-112 (median 13) |

DXRT=Deep X-ray therapy
* $p<0.01$ Wilcoxon signed rank

### 7.3.1 Endoscopic

All patients seen for 'check endoscopy' had good symptom control at that time. Eight had minimal or no tumour present at endoscopy and the endoscope passed through the stricture with no difficulty. (None of these patients required more than 2,000J laser treatment at this time). Further procedures were performed when recurrent symptoms occurred (median every 13 weeks range 6-112 weeks). Two patients had tight strictures with obvious tumour shrinkage. The stricture was clearly infiltrated with tumour in both these patients and further laser therapy was required in order to pass the endoscope above the level of the stricture. These 2 required regular follow up to prevent them obstructing. Three patients declined to come for a 'check' endoscopy immediately following radiotherapy as they had no bowel symptoms. Two of them never required further endoscopy as their local bowel symptoms remained well controlled (survival 2.5 and 14 months). The third, a 69 year old patient with an inoperable rectosigmoid cancer, underwent further laser therapy 10 months after radiotherapy when she developed recurrent rectal discharge. This was controlled with 5,000J laser energy after which the patient had no further rectal symptoms to death 6 months later. {She did however also have some chemotherapy the details of which are unknown}.

### 7.3.2 Symptomatic

Laser therapy was considered to be successful if symptoms caused by intraluminal tumour were reduced to an extent that enabled the patient to lead a lifestyle appropriate to his or her age and general condition without constant concern for bowel function. Initial laser treatment had been successful and bowel symptoms were well controlled for the first two months following radiotherapy in all patients. Long term success (to date or to terminal period) was achieved in 11/13 (85%) patients. The results in figures 7.2 and 7.3 show a dramatic resolution of rectal bleeding and diarrhoea. The initial assessments were made after laser and the final ones represent and average figure for the remaining lifetime but the terminal few weeks were excluded. Overall there was a further small improvement in these symptoms with additional radiotherapy. Patients with additional symptoms such as tenesmus or obstructive symptoms were more likely to have residual symptoms. This may be due to a loss of rectal capacity.

One of the patients with bleeding and Tenesmus was asymptomatic for almost 12 months but in the terminal 2 months suffered with perineal pain and fecal incontinence. One of the long term failures was a demented 81 year old man who presented with obstructive symptoms and bloody rectal discharge and was found to have a circumferential rectal lesion. He did well for a year before developing intermittent rectal incontinence. This may however have been partly related to his dementia as the tumour appeared controlled endoscopically.

The second failure occurred in a 77 year old male who presented with severe secretary diarrhoea (15 motions per day), hypokalaemia, hyponatraemia and pre-renal failure. He was found to have a 14cm circumferential villous adenoma but no focus of malignancy was detected on repeated biopsies. Surgical resection proved impossible after he had a cardiac arrest on the operating table. He underwent 11 laser procedures prior to radiotherapy which controlled the discharge and fluid and electrolyte loss and the tumour length shrank from 14cm to 8 cm. However laser procedures were required every 4 weeks. Initially symptoms were well controlled after radiotherapy but the mucus discharge became troublesome again after 2 months. The patient was very reluctant to have further surgery but eventually agreed. The second procedure went smoothly (as the fluid and electrolyte problems remained controlled after laser and radiotherapy treatment), an abdomino-perineal resection was performed and the patient remains well 27 months later. Histology of the surgical specimen showed no cancer.

### 7.3.3 Treatment requirements

Whenever possible laser and radiotherapy were performed on an out patient basis though many patients came from long distances so radiotherapy had to be given as an in patient. Time in hospital ranged from 0-52 days (median 20 days). Overall the number of laser treatments required ranged from 1-20 (median 5). The number before radiotherapy was 1-9 (median 2) and after radiotherapy 0-11 (median 3). The laser treatment intervals required to control symptoms are shown in table 2. The 'before' radiotherapy treatment intervals are given for the patients who were followed for 3 months or more while undergoing laser. This period was chosen as it was felt that this was the minimum period required to obtain a good baseline for treatment frequency and laser energy requirements for good tumour control. The initial treatment intervals start from the time of completion of the initial recanalisation, whether this took one or more treatments. Some patients were brought back routinely 4 weeks after recanalisation and most 4-8 weeks after radiotherapy. The routine checks distort the data to some extent but since checks were performed both before and after radiotherapy the bias is minimised. The figures show a dramatic increase in treatment interval from 4 weeks before treatment to 14 weeks after, the treatment interval for 'C2' tumours being longer that that for 'C3'. In terms of laser energy required to control symptoms {excluding initial recanalisation (table 7.3)} there was also a dramatic reduction in the figures per month required before and after radiotherapy indicating a corresponding reduction in the regrowth rate of intraluminal tumour bulk. ($p<0.01$).

### 7.3.4 Survival and Complications

To date 12/13 (92%) of the patients in this study have died, survival in this group was 2.5-28 months (median 15 months). No serious endoscopic complications occurred. Radiotherapy was generally well tolerated. One patient suffered with transitory lethargy during treatment which may have been radiotherapy related. Four patients developed fibrous/neoplastic strictures following radiotherapy. All were dealt with endoscopically except one who required a diverting colostomy after 13 months of successful treatment. Another, in a 91 year old with inoperable rectal cancer, was particularly 'tight' and required frequent follow up laser treatment every 6 weeks. She eventually died after 14 months successful treatment with severe cachexia and large bowel obstruction. At the end, her general condition was felt to be too poor to justify a defunctioning colostomy.

**Table 7.3 Laser energy requirements before and after radiotherapy (excluding initial recanalisation)**

| | *Laser energy (C2 tumours)* median (range) | *Laser energy (C3 tumours)* median (range) | *Laser energy (all tumours)* median (range) |
|---|---|---|---|
| **J/month pre DXRT** (7 patients followed for > 3 months prior to DXRT) | 5,000 (2,500-13,000) | 22,000 (5,000-26,000) | 15,000 (2,500-26,000)* |
| **J/month post DXRT** (7 patients as above) | 800 (0-2,000) | 3,500 (0-8,000) | 2,000 (0-8,000)* |
| **J/month post DXRT** (all 13 patients) | 0 (0-2,000) | 800 (0-8,000) | 700 (0-8,000) |

*$p<0.01$

## 7.4 Discussion

Laser therapy is now an established treatment in many units for palliation of symptoms in patients with inoperable rectal cancer. It is effective in 80% and is a particularly gentle and safe treatment not requiring general anaesthesia and carrying a low risk of serious complications. The problem of the need for frequent follow up procedures is however a major one as this is inconvenient and sometimes distressing for the patient. Laser treatment can be technically difficult, particularly in patients in whom the endoscope will not pass the stricture. It usually takes longer than with oesophageal tumours and constitutes a considerable workload. This small pilot study demonstrates promising results for the combination of laser and radiotherapy in rectal and rectosigmoid cancer. The treatments should be complimentary, laser to gain rapid relief of troublesome discharge and obstructive symptoms and radiotherapy to address the entire tumour bulk, and this appears to be confirmed. In addition endoscopic therapy has the advantage of pre-empting the obstruction which may result from radiotherapy. Both endoscopic and symptomatic results were impressive. Only two patients in this study failed to achieve long term functional success. The patient with the villous adenoma had a very extensive lesion which was initially 14 cm long and it was a notable success to control his troublesome rectal discharge at all. Even he had definite symptomatic and endoscopic benefit from additional radiotherapy and his general condition improved enough for him to undergo successful surgery. The reduction in follow up procedures to one every 42 weeks or so for C2 tumours and 9 weeks or so for C3 tumours is a useful improvement in follow up requirements. The reduction in laser energy per month required for good symptom control is another indicator which suggests benefit from radiotherapy. Only 12 of 32 patients referred with rectal/rectosigmoid cancer who received laser therapy during the 18 month period were entered into this study. We were reluctant to submit patients with very poor prognosis to a 2 week course of radiotherapy and the small proportion entered reflects the extent of disease and poor general condition in this elderly group who are referred for laser treatment. The median survival of a year or more with symptoms controlled in most of those treated represents a very satisfactory outcome. Despite the development of radiation strictures in 3 patients none required open surgery. All were controlled for long periods with endoscopic treatment although it is possible that obstruction contributed to death in one patient. There are several other treatments available for palliation of rectal and rectosigmoid cancer; these include electrocoagulation , transanal resection and cryotherapy . These are reviewed in more detail in chapter 2. They are all more aggressive than treatment with laser and carry a higher risk of complications and only cryotherapy can be performed without general anaesthesia. All of these treatments however suffer from the same inability to reach tumour outside the bowel wall. It is likely that combination of these modalities with radiotherapy might also be complimentary. To further clarify the benefit of the combination of topical techniques for tumour destruction and external beam radiotherapy randomised studies are required.

# CHAPTER 8

## A CUFFED TUBE FOR PALLIATION OF COMPLICATIONS OF OESOPHAGEAL MALIGNANCY AND ITS TREATMENT WITH LASER/RADIOTHERAPY

### 8.1 Background

Following a favourable report using Ivalon sponge wrapped around an Atkinson tube for malignant oesophago-respiratory fistulae (Robertson 1986) the 'cuffed' tube was designed exclusively for this purpose. These fistulae present a difficult and distressing complication of mediastinal cancer which untreated, is rapidly fatal. Presentation is often acute and is manifested by severe bouts of coughing when food or fluids are taken by mouth and by recurrent pulmonary infection and collapse. There have been case reports (Lacey Smith 1987, Irving 1988, Spinelli 1989) of satisfactory treatment of fistulae with the cuffed prostheses but no more than 2 patients are included in each.

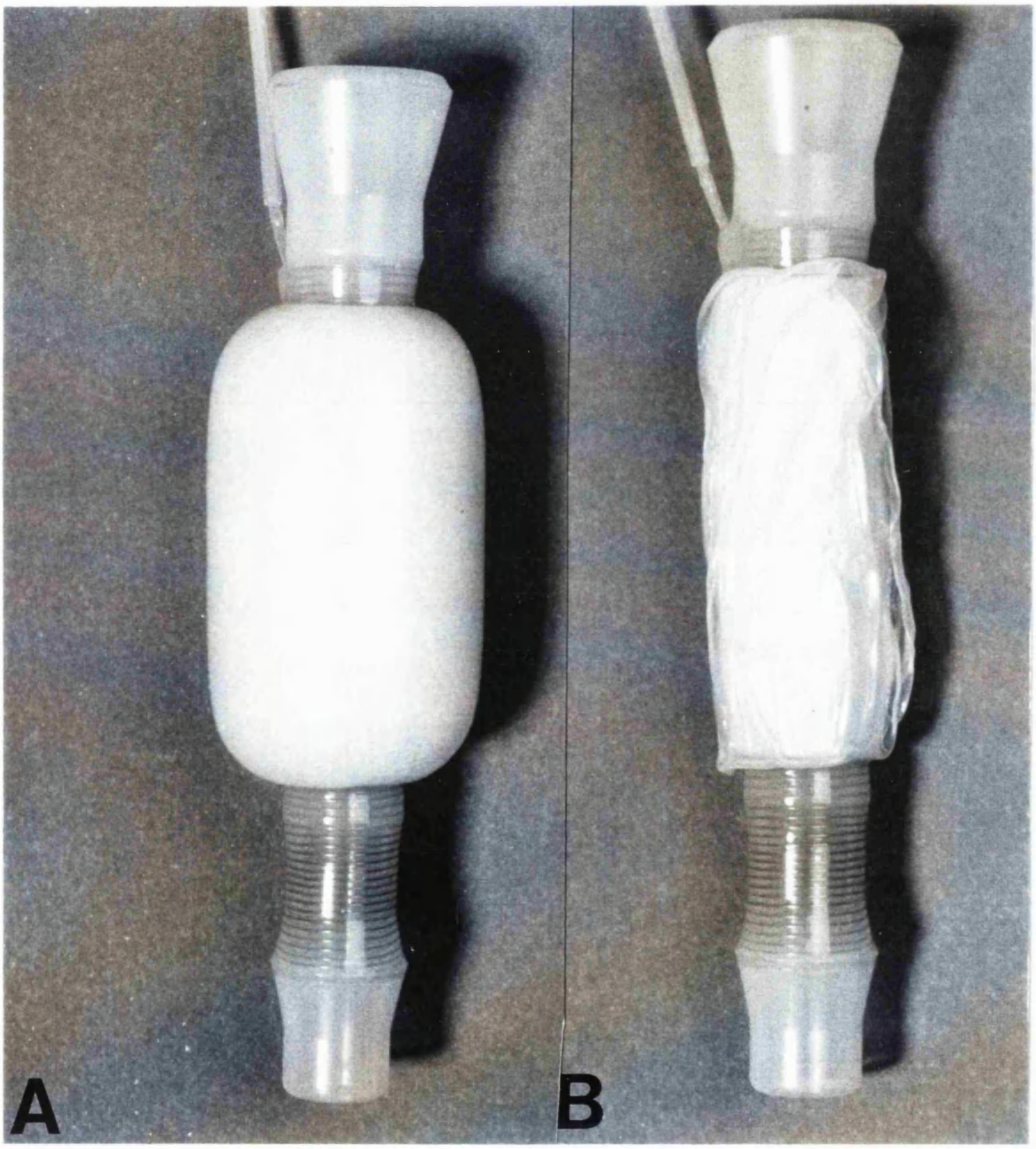
Most of our patients are tertiary referrals and thus one would expect a high level of complicated or difficult cases. We first obtained cuffed Wilson-Cook oesophageal endoprostheses (William Cook Europe Limited) in early 1990 and in the subsequent 2 years we have used them in the 15 cases with oesophageal cancer described. Nine had oesophago-respiratory fistulae. In addition to treatment of this group of patients we have found these tubes invaluable in certain difficult if not desperate situations in oesophageal malignancy which are described.

### 8.2 Methods

The prosthesis (figure 8.1) is a standard Wilson Cook silicone rubber tube containing a metal coil with soft silicone rubber ends.

Figure 8.1

A 10.4cm (shaft) Wilson -Cook cuffed tube with the cuff inflated (A) and deflated (B)ready for insertion.



The cuff is formed by a layer of foam rubber wrapped around the shaft of the tube which is surrounded by a thin sheath of silicone rubber. The foam inside the cuff will self inflate if allowed. It is deflated immediately prior to insertion (figure 8.1) by means of a plastic cannula which inserts into the cuff and is attached to a 50ml syringe. When satisfactorily positioned with the fistula at the mid point of the cuff the balloon can be inflated with air before the cannula is 'pulled' out of the cuff prior to freeing of the tube from the introducor. The cuff will however 'self inflate' once the cannula is removed but we have found that inflation with a syringe is not really necessary (and may cause respiratory distress). The soft foam contours the shape of the oesophagus once in situ to a maximum diameter of 36 mm (deflated diameter of 23mm). The tubes come in several sizes but the cuff is located at the top of the shaft and is positioned the same distance from the top of the tube (3cm approx) for all sizes. All tubes have a soft funnel at the proximal end which is 2.5cm long and a distal funnel (to help stop upward displacement) which is 2 cm long. The tubes are sold according to shaft length (4.4 to 16.4 cm in 2 cm increments) and thus the total tube length is 4.5cm longer than this. The price at the time of writing is £158.

Patients are intubated under sedation with diazemuls/pethidine using endoscopic and fluoroscopic control. Transcutaneous pO2 monitoring is routine. The oesophagus is usually dilated to 18 mm with Celestin dilators prior to tube insertion; some patients with fistulae do not have strictures in which case dilatation is not performed. We use an Atkinson introducer to place these tubes which grips them nicely and saves the expense of an additional Dumon-Gilliard introducer which is recommended for insertion. Extra care is required when endoscoping these patients as secretions and debris in the oesophagus can easily enter the airways and cause respiratory distress. It is important to suck such secretions up the endoscope before this occurs. It is also advisable to have sedation reversing agents (naloxone/anexate) readily available should they be required. One patient developed acute respiratory distress shortly after intubation with a cuffed prosthesis which had to be removed. This can occur with conventional prostheses (particularly when used for tumours of the cervical oesophagus), however this may be more likely to happen with a cuffed tube as it is possible for the cuff to protrude through the fistula and obstruct the bronchus concerned. It is thus important that there is a coordinated team approach with appropriate equipment available to rapidly remove the tube if necessary.

## 8.3 <u>Results</u>

### 8.3.1 <u>Oesophago-respiratory Fistula.</u>

#### 8.3.1.1 <u>Patient details</u>

Patients with fistulae are documented in table 8.1 and endoscopic photographs of a fistula is shown in figure 8.2; 8 fistulae occurred in the thoracic and 1 in the cervical oesophagus. All patients suffered with coughing when swallowing fluids prior to intubation. Six fistulae were demonstrated radiographically, one of which (case 6) could not be seen at endoscopy. The other 3 (cases 2, 3 and 5) were demonstrated at endoscopy on presentation and cuffed tubes were inserted at the same procedure. Only one patient had not undergone radiotherapy or laser treatment prior to the development of a fistula and 2 patients had received both.

Success was deemed as the abolition of coughing with swallowing, confirmation of fistula closure with a contrast swallow and the ability to take a soft diet for the remaining survival period. Using these criteria 5 cases were regarded as completely successful and 4 cases were only partially successful. Two of these patients who initially did well suffered with a recurrence in symptoms from tube displacement, one tube kept slipping despite 2 attempts at repositioning (case 3). One patient was only able to swallow fluids despite closure of the fistula and another died of bronchopneumonia (established prior to the procedure) 48 hours after the procedure after swallowing fluids only.

#### 8.3.1.2 Case Report A

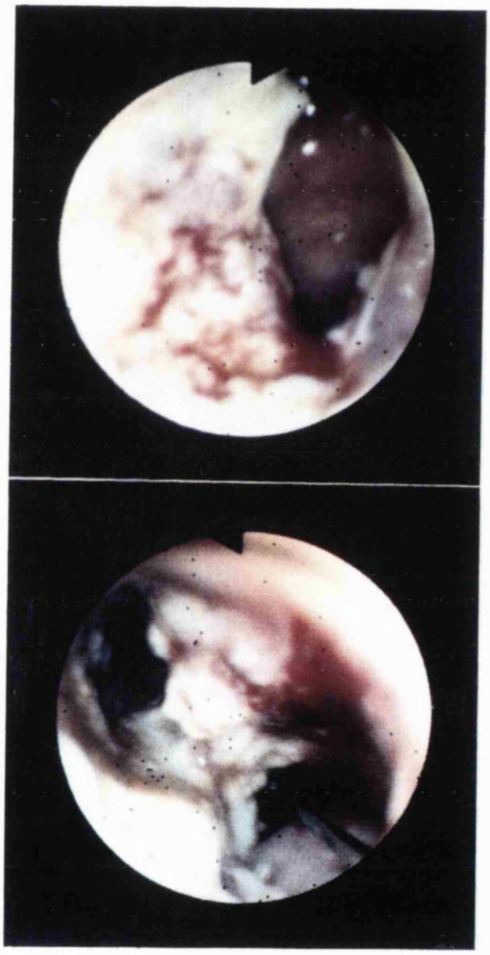
A previously well 61 year old man presented with dysphagia and was found to have a squamous cell carcinoma at 25-30 cm from the teeth. A C-T scan showed thickening of the oesophageal wall on the right anterolateral aspect from just below the level of the sternoclavicular joints to the level of the carina. The mass was contiguous with the posterior aspect of the trachea and the anterior aspect of the aorta and was thus thought to be unresectable. He was referred for radiotherapy and received a dose of 60Gy in 20 fractions over 4 weeks. Dysphagia improved during this period to allow some solid food to pass but after a further month his swallowing was deteriorating again and he was referred for laser treatment. Over the following 15 weeks excellent swallowing was maintained with dilations and laser (3 procedures). The patient then developed coughing on swallowing liquids and was found to have a fistula at the top end of the tumour. A 15 cm Celestin tube was placed through the stricture to cover the fistula but unfortunately a contrast swallow showed contrast was flooding around the tube and through the fistula. The Celestin tube was removed and a 10.4cm (shaft length) cuffed tube was inserted which closed the fistula allowing the patient to eat soft foods. He was discharged after 10 days and lived a total of 9 weeks after cuffed tube insertion .

Table 8.1 Patients with fistulae

| No | Nature | Histology | Sex | Age | Previous DXRT | Previous laser | Teeth to tumour | Fistula | Success | Survival | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Oesophageal | Squamous | M | 61 | Yes-60Gy | Yes-3 treatments | 25-30cm | 25cm | Yes | 9/52 | Case report A |
| 2 | Oesophageal | Squamous | M | 48 | Yes-45Gy | No | 26-40cm | 38cm | Yes | 3/52 | 2 fistulae-previous celestin tube ineffective |
| 3 | Oesophageal | Squamous | M | 69 | No | Yes-3 treatments | 23-27cm | 25cm | Partial-3/52 | 6/52 | Tube slipped and could not be repositioned |
| 4 | Oesophageal | Squamous | F | 49 | Yes-30Gy | Yes-3 treatments | 20-25cm | 21cm | Partial | 4/52 | Only swallowing fluids |
| 5 | Oesophageal | Squamous | F | 81 | Yes 20Gy | No | 20-28cm | 25cm | Yes | 13/52 | Schizophrenic lady. |
| 6 | Bronchial | Anaplastic | M | 51 | Yes-20Gy | No | 30-50cm | Not seen | Yes | 2/52 | Fistula only demonstrated with radiology |
| 7 | Bronchial | Squamous | M | 57 | Yes-30Gy | No | 29-35cm | 30cm | No | 48 hrs | Died of bronchopneumonia 48hrs after procedure |
| 8 | Bronchial | Non small cell | M | 62 | No | No | 23-29cm | 23-29cm | Yes | 6/52 | |
| 9 | Oesophageal | Squamous | F | 57 | Yes-60Gy | No | 20-25cm | 20cm | Yes with Celestin tube | 2/52 | High fistula, respiratory distress with cuffed tube |

**Figure 8.2 A and B. An example of an oesophagorespiratory fistula.**

(The wire in B has been passed into the stomach prior to tube insertion)



### 8.3.2 Oesophageal perforation/tear

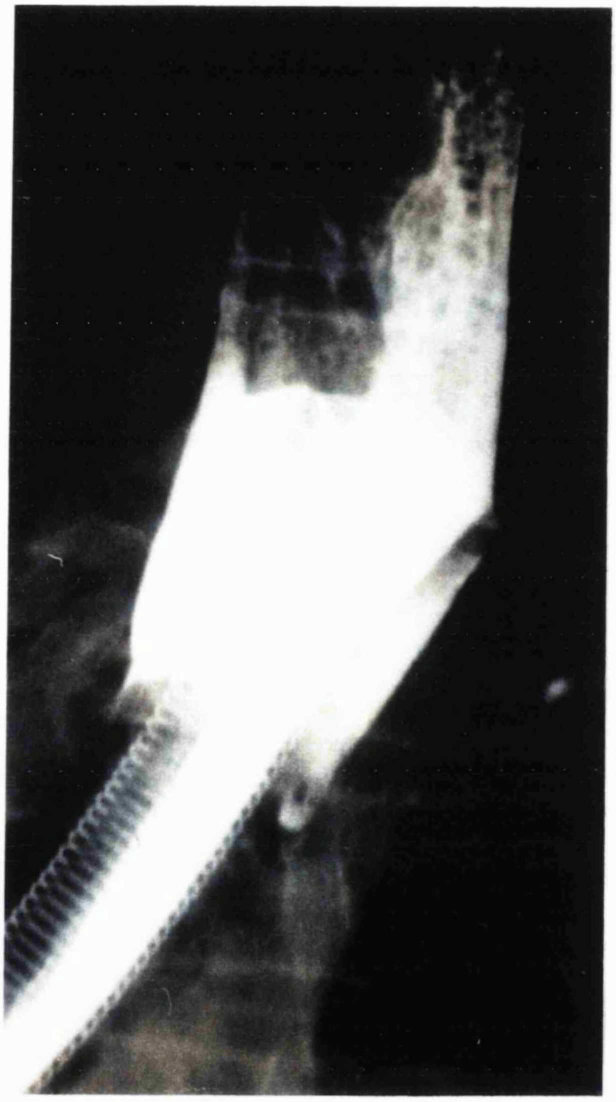
In the past we have elected to intubate such patients with conventional tubes but we believe cuffed tubes may allow a more rapid re-introduction of oral intake.

#### 8.3.2.1 Case report B

An 80 year old lady was referred by her General Practitioner with a 1 month history of dysphagia for solids. At endoscopy she was found to have a 4 cm mid thoracic lesion which was subsequently found to be a squamous cell cancer. The stricture was tight and the endoscope would not pass. Following insertion of a wire the stricture was dilated under screening; initially with the 11mm Celestin dilator and then the 18mm Celestin dilator. Following dilatation the tumour was seen to have split along its full length and the pleural cavity could be seen. The patient developed surgical emphysema and a cuffed tube was immediately inserted across the perforation. Intravenous antibiotics were given for 3 days and then converted to oral for a total of 7 days. A contrast swallow 24 hours later showed mediastinal air but no leak. A soft diet was commenced and the patient was discharged 6 days later. She has remained well on a semi-solid diet and eventually died 10 months later.

**Figure 8.3**

Case report B. A cuffed tube was inserted and this contrast swallow performed afterwards shows no mediastinal leak. Contrast floods around the tube and stops abruptly at the level of the cuff. Air can be seen in the partially inflated cuff.



### 8.3.3 Group 3 Life threatening bleeding

Arterial spurting from tumours is not common but is occasionally laser induced as in the first 2 of our cases. All the cases treated had adenocarcinomas of the cardia. The first 2 were localised tumours but the third case had an extensive tumour 11cm long. Cuffed tubes were highly effective for controlling bleeding in all cases. The first 2 swallowed well and lived for a prolonged period. The last case was a man with an extensive tumour who was dying. The tube however allowed him a peaceful demise without haematemesis and able to swallow liquids.

#### 8.3.3.1 Case report C

A 75 year old man with an unresectable adenocarcinoma of the cardia and aortic stenosis was referred for laser treatment following a laparotomy. He had presented with a 2 month history of dysphagia and weight loss and was found to have a large tumour at the cardia. At laparotomy the tumour mass was found to be arising from the lower oesophagus and was firmly fixed posteriorly. There were also tumour nodules in the gastro-hepatic omentum and thus no attempt at resection was made. Initial laser recanalisation for a predominantly polypoid tumour (38-41cm from the teeth) was performed in a total of 5 sessions. An excellent lumen was achieved and the patient was able to manage most solids with monthly laser treatments. Three months later at a routine laser treatment fresh blood was found in the stomach and an arterial spurter was identified at endoscopy at 40cm from the teeth (tumour 35-42cm). Bleeding was stopped with laser and injection of 8mls of 1:10,000 adrenaline. The haemoglobin was 8.3 grammes and following a 4 unit blood transfusion the patient was discharged. One week later, he had a severe episode of haematemesis and melaena and was admitted to a local hospital in shock with a haemoglobin of 4. Five units of blood were transfused and he was transferred back to us after another week. At that time further active bleeding was found from the same site for which a further 3 units of blood were transfused. We elected to insert at 10.4cm (shaft) cuffed tube with the centre of the cuff at the level of the spurter. Following this procedure the patient lived a further 6 months, his haemoglobin remained normal and he required no more blood transfusions.

**Table 8.2 Patients treated for oesophageal perforation or tear**

| Nature | Histology | Sex | Age | Length | Perforation | Survival | Comments |
|---|---|---|---|---|---|---|---|
| Cardia | Adenocarcinoma | F | 63 | 5 cm | Y-surgical emphysema | 6/52 | Died suddenly swallowing well |
| Thoracic oesoph | Squamous | F | 80 | 4cm | Y-surgical emphysema | 40/52 | Swallowed semi-solids until death |
| Cardia | Adenocarcinoma | F | 74 | 3cm | N-Tear after tube removal | 10/52 | Swallowed semi-solids to death |

**Table 8.3 Patients treated for life-threatening bleeding**

| Tumour | Age | Sex | Laser induced ? | Transfusion Req | Success | Survival |
|---|---|---|---|---|---|---|
| Adenoca Cardia | 84 | F | Yes-acute | 2 units in 4 hours | Yes | 15 weeks |
| Adenoca Cardia | 75 | M | Yes-Initially | 11 units in 2 weeks | Yes | 26 weeks |
| Adenoca Cardia | 71 | M | No | 4 units in 1 week | Yes | 1 week |

## 8.4 Discussion

There are 3 main aims in the treatment of malignant oesophago-respiratory fistulae. These are i) To exclude oesophageal contents from the respiratory tract. ii) To restore swallowing as well as possible and iii) to carry an acceptable morbidity and mortality. Surgical management is fraught with problems. A variety of surgical bypass techniques have been described using stomach or colon for interposition using a presternal or substernal approach (Mannell 1980, Wong 1981, Duranceau 1984). This type of surgery is highly invasive and the poor general condition of these patients results in a high mortality (30-40%) and incidence of local complications. These figures are not acceptable for treatment of incurable patients and hence the need for less invasive therapies. Surgical exclusion alone is one option but combined cervical oesophagostomy and gastrostomy still carries a 10% mortality (Duranceau 1984) and does not allow the patient to swallow. Endoscopic techniques are able to fulfil the 3 aims in the treatment of these patient. Survival in this group is limited (median 4 weeks in this series).

All but one of the fistulae were associated with prior laser or radiotherapy and this association has been noted by other authors (Buess 1988). Unfortunately pressure necrosis from standard prosthetic tubes can also be responsible for this complication and thus intubation of patients known to have tumour adjacent to an airway is not necessarily a way of avoiding this problem. Conventional tubes may allow ingested material to pass along the side of the tube and through the fistula (case A) and other reports have documented this problem (Irving 1988, Buess 1988). The effect of the cuffed tube is well demonstrated by fig 8.3 which shows contrast passing down the side of a tube and stopping dead at the cuff. It is not uncommon for fistulae to occur in the absence of a stricture and the problem of tube migration is largely avoided with a cuffed tube in these cases.

The important published data with oesophageal prostheses for fistulae is summarised in table 8.4. In some of the publications 2 or more types of tube have been used in these patients and it is difficult to determine which results have been achieved with which tubes. Authors using various modified prostheses appear to have achieved results similar to ours although 'standard' prostheses probably only close fistula at the first attempt in about 50% of patients. The technique of Ivalon sponge wrapping (Robertson 1986) in 4 of the 11 tubes inserted fully closed 8 of 11 fistulae and 10 of the patients left hospital. All but one managed a semi-solid diet. Median survival was 8.5 weeks. Another report (Buess 1988) advocated a modified tube with a large upper funnel (fistula funnel) for these patients. Twenty one patients with fistulae were studied although only 3 were intubated with these modified tubes; 18 were 'successful' but only with a tube change in 6 patients. Median survival was 6 weeks. These tubes may offer an advantage over the cuffed tube in patients with high fistulae. The problem with using a cuffed tube in this situation is that the full diameter of the cuff starts only 4 cm from the top of the tube and thus when the cuff is placed at the level of the fistula the top of the tube protrudes into the back of the throat and may not be tolerated. We have found a similar device useful in treating high cervical lesions (Loizou 1992); 3 of the 8 patients so treated had fistulae which were sealed. However for lesions in the thoracic oesophagus it is surprising that such an approach is effective as there is often marked oesophageal dilatation proximal to a stricture.

Patients with oesophageal malignancy who have undergone laser/radiotherapy combination treatment may be more likely to suffer with instrumental perforation (chapter 4). In the past it has been our practice to intubate them immediately with conventional tubes but we were very cautious in restarting oral intake, particularly in patients with long tears. We usually waited 4 or 5 days before requesting a contrast swallow. Use of a cuffed tube allows more rapid re-introduction of oral intake. All 3 patients had contrast swallows and were started on fluids within 48hrs of the trauma and were discharged within a week. Use of a tube with a 'fistula funnel' would probably also suffice for such lesions. We have treated one patient with a very high perforation (1 cm below the chords) with a similar tube with a large floppy funnel (Loizou 1992). The perforation occurred following dilatation of a tight fibrous stricture (and recurrence) consequent on prior radical radiotherapy for a squamous cell cancer. The perforation was nicely sealed with the modified tube and the patient swallowed a semi-solid diet and survived 4 months.

Severe bleeding from oesophageal cancers can be extremely difficult to control. Arterial spurters in malignant tissue often do not respond to injections or laser as well as similar vessels in peptic ulcers. Such cases present a real dilemma as to suffer recurrent haematemesis and bleed to death is a particularly unpleasant demise for patients who are often alert. The 2 who went on to survive several months were both bleeding severely and may well have died from bleeding if they hadn't been intubated. We found cuffed tubes invaluable for these patients for whom there is no alternative.

We have found cuffed tubes invaluable in the 3 groups of patients discussed. Even when the prognosis is poor these tubes have something to offer both in terms of prolonging life in some cases but equally importantly in palliating miserable symptoms and allowing a dignified death.

## Table 8.4

## Published series of oesophageal prostheses for the treatment of fistulae

| Authors | Tube | Patient No | Success | Survival (Median) | Comments |
|---|---|---|---|---|---|
| Robertson 1986 | Atkinson & ISR Atkinson | Total 11<br>6 At *<br>5 ISR At ^ | 8/11 (72%) | 8.5 Wks | 1 died post procedure<br>3 fistulae not closed |
| Davidson 1986 | Atkinson | 6 | 4/6 (66%) | 10 Wks | 1 died post procedure<br>1 fistula not closed |
| Buess 1987 | Various<br>Eska Buess +Fistula funnel | Total 21<br>3 | 18/21 (85%) {but 6 tubes changed} | 6 Wks | 2 died post procedure<br>1 fluids only |
| Lux 1987 | Cuffed WC tube | 1 | Yes | - | Case rpt |
| Irving 1988 | Cuffed WC tube | 2 | Both | 'some Wks' | Case rpts |
| Loizou 1992 | 'Modified' Celestin | 3 (cervical) | 2/3 | 6 Wks | 1 swallowing little |

* At = Atkinson tube

^ISR At = Ivalon sponge wrapped Atkinson tube

# CHAPTER 9

## RECANALISATION OF TUBE OVERGROWTH : AN ADDITIONAL USE FOR LASER IN PATIENTS WHERE LASER AND/OR RADIOTHERAPY HAS PREVIOUSLY FAILED

### 9.1 Aims and rationale

Oesophageal prostheses are an effective and often life long method of relieving dysphagia in patients with cancers of the oesophagus and gastric cardia. The quality of swallowing is not always as good as after laser. We advocate routine use of tubes in patients who are unsuitable for laser, who fail to swallow well with laser at any stage of treatment, or who develop complications not treatable with laser (chapter 8). In the randomised study of laser and laser with radiotherapy (chapter 3) 25/67 patients (37%) were eventually intubated. There may be a small increase in the percentage of those requiring intubation in patients receiving radiotherapy but the randomised study was not big enough to determine this. It is also important to note that many units do not have access to laser facilities and most patients in the UK are palliated by intubation as first line treatment. As discussed in chapter 2 15%-50% of patients suffer tube complications or malfunction. Perforation at intubation occurs in up to 11% of patients and late perforation in up to 7%. Tube blockage and migration are the most common late complications. Food bolus obstruction can usually be cleared with ingestion of carbonated fluids or of a small quantity of hydrogen peroxide diluted in water. If this fails the tube can be cleared endoscopically. Migration occurs less frequently (3%-19%) and requires tube repositioning or replacement although some of these patients may be better managed with laser treatment. Tube overgrowth occurs in a small but significant number of patients and is often difficult to deal with. The incidence of tube overgrowth varies between series but most authors document such cases. Ogilvie (1982) recorded 7 cases in 118 patients (6%) but Gasparri (1987) described only 5 cases in 248 intubated patients (2%). In our own study of laser versus tube overgrowth was seen in 2/30 (7%) of those intubated. Patients usually present with this problem many months after intubation and the value of further therapeutic measures has not been determined. We undertook this prospective study to assess the value of laser therapy in this group.

## 9.2 Methods

### 9.2.1 Patients

We studied 14 patients with tube overgrowth seen in this unit between December 1986 and April 1991. Twelve patients had been intubated at other centres and 2 had overgrowth following intubation by us. Tube position had been documented endoscopically in all patients after insertion. All patients were rescoped when they developed overgrowth and assessment of their tubes at that time confirmed none of them had become displaced. All patients with displaced tubes were excluded.

The median patient age was 75 (range 46-90), 11 were male and 3 female. Eleven patients had adenocarcinomas and 3 squamous cell carcinomas. Twelve tumours were in the lower thoracic oesophagus or cardia and 2 patients had anastomotic recurrences following previous surgery. It is unusual for such patients to undergo a second resection in the UK. Ten patients were deemed unsuitable for surgery due to age and general condition and had been intubated endoscopically. Two had been found to have inoperable tumour at laparotomy and a tube had been inserted during the operation (and sewn in). Nine tubes were Celestin and 5 Atkinson in design. All patients were well palliated immediately following tube insertion; all were able to manage a semi-solid diet or better. The median time from intubation to referral with an overgrown tube was 7 months (range 4-14 months). Eleven tubes were overgrown at the top, 2 at the bottom and 1 at both ends. The median length of the tumour beyond the end of the tube was 3cm (range 2-5cm).

### 9.2.2 Techniques

The general laser technique has been discussed in detail in chapter 1. Overgrown areas are often polypoid and it is safe to vaporise nodules shaving them back to within 2-3 millimetres of the oesophageal wall. Raised flat areas of tumour can be coagulated and will slough within a few days of treatment. It is usual practice to commence laser treatment at the distal end of the tumour and proceed proximally as laser induced swelling may prevent passage of the scope. Overgrown tubes cannot usually be negotiated with the scope and thus treatment normally has to be started at the proximal end. This does not usually cause a problem as overgrown segments are short and following vaporisation of nodules the scope will often pass through the stricture at the end of one session. Tubes overgrown at the bottom require a smaller calibre endoscope as the Olympus 1T 20 endoscope (KeyMed Ltd, Southend UK) normally used for laser treatment will not pass through either Atkinson or Celestin tubes. Angulation of the endoscope while confined within the tube is limited and targeting can be more difficult than similar growths above the tube. In order to achieve the best lumen some patients also underwent tube manipulation and one had a second tube inserted above the first, the details of this are given below. All tube manipulation was performed with an Atkinson introducer. This presented no problem for Atkinson tubes but as Celestin tubes have a slightly larger internal diameter it was sometimes necessary to wrap some micropore tape around the olive at the distal end of the inserter to allow enhanced grip on the tube. Even with this technique it was often not possible to grip these tubes sufficiently tightly from the inside particularly if the tumour was very hard and the tube had been in position for several months. In these cases greater force could be applied to pull a tube up if the plastic olive of the inserter was opened below the bottom of the tube. However, if this is done the endoscopist must be prepared to remove the tube as on one occasion, in a patient with a displaced tube, (not discussed in this series) the plastic olive jammed in the bottom of the tube and could not be separated. All patients were assessed prior to and directly following treatment and there dysphagia grades recorded as discussed in chapters 4 and 5 while still in hospital and subsequently by telephone. The mean dysphagia grade for each individual during follow up was used in the analysis.

### 9.2.3 Statistics

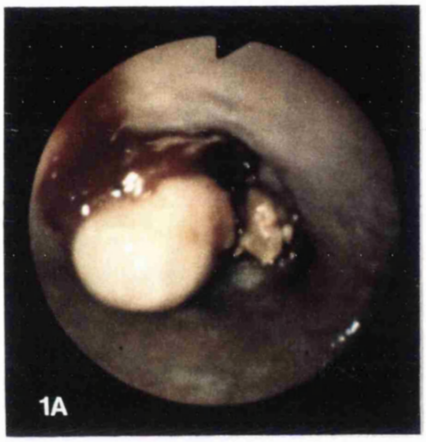
Dysphagia data were assessed using the Wilcoxon Signed Rank test for paired data.

## 9.3 Results

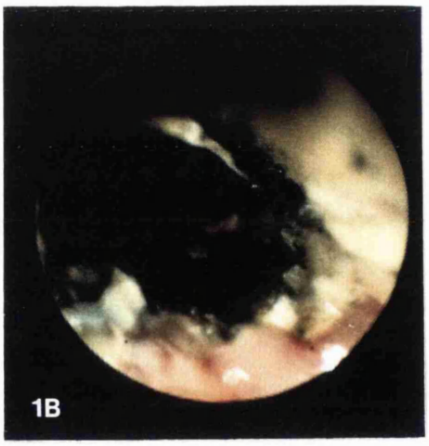
Three examples of tube overgrowth are shown (see Figures).

**Figure 9.1**

**A)** This is a typical polypoid tumour overgrowing a Celestin tube in an 83 year old man who presented with recurrent dysphagia 14 months after tube insertion for an adenocarcinoma of the cardia.

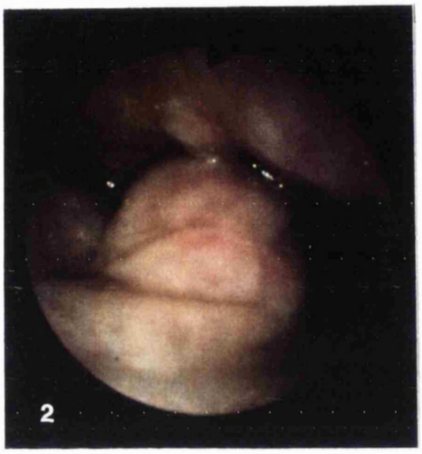



**B)** This demonstrates the result following laser of the tumour shown in figure 9.1A.




This tube was one of those shifted up (in this case by 5 cm) to entirely cover the overgrown area. A further overgrowth occurred and the patient required repeat laser treatment 20 weeks later but he survived a total of 36 weeks after the first laser treatment. He was swallowing a semi-solid diet for almost all that time.

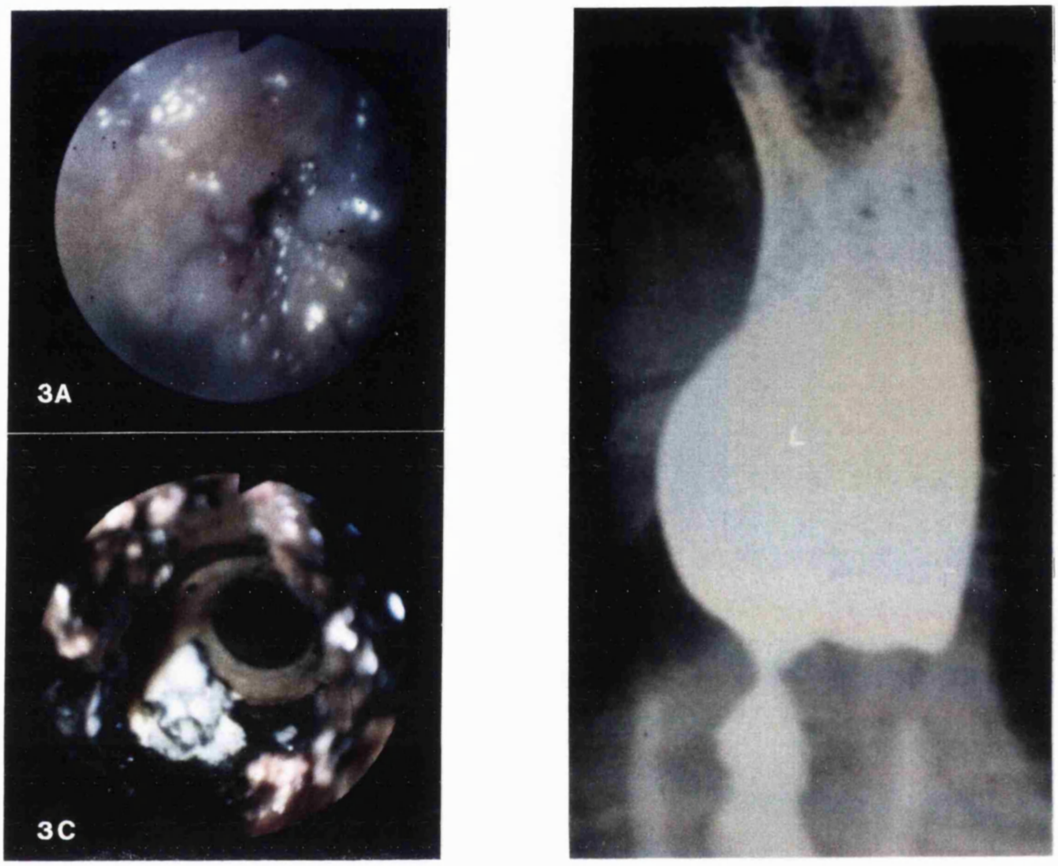
## Figure 9.2




Some overgrowths are not so easily recognised. This shows what may have been dismissed as a fold of normal mucosa or oedematous swelling resulting from pressure necrosis. This appearance occurred above an Atkinson tube which had functioned well for 7 months for a 79 year old lady with an adenocarcinoma at the cardia. The lesion could not be passed with the endoscope and had a hard 'tumour like' consistency. It was treated, tentatively at first, with laser. As treatment progressed the 'fold' was seen to be obviously neoplastic and a considerable amount of laser energy was applied (18,000 Joules) to vaporise the whole area and to give good palliation.

We would stress that extreme care must be taken when treating such lesions. If there is doubt about the nature of such a lesion it may be safer to resort to tube manipulation or replacement instead.

## Figure 9.3




A) This shows the appearance of tumour overgrowing an Atkinson tube which had provided good palliation for 9 months in a 75 year old man with an adenocarcinoma of the cardia. In this case there is a diffusely abnormal mucosa with a pin point lumen through the middle.

B) This is the barium swallow prior to laser in the patient whose tumour is shown in figure 9.3A. There is a trickle of contrast passing through the stricture just above the top of the tube. The area around the lumen was vaporised to reveal obviously neoplastic tissue and this was shaved back with laser to reveal the tube as shown in figure 9.3C.

C) Post laser appearances of tube overgrowth show in figure 9.3A. This man could swallow nothing before laser treatment but was discharged swallowing semi-solids. His condition deteriorated fairly rapidly but he was still able to swallow fluids when he died 8 weeks later.

The 11 patients with overgrowth at the top of their tubes only were all treated with laser but 3 also underwent tube manipulation using an Atkinson introducer following laser. The 3 tubes shifted were moved up to completely cover the overgrown area and further treatment was only required in one (case history 1). All 11 patients swallowed a semi-solid diet for most of their survival.

Two patients with tumour distal to the tube only underwent laser treatment. One was lasered using an Olympus XQ 10 endoscope through the tube. Another was palliated by shifting the tube down with an Atkinson inserter to cover distal tumour; this uncovered tumour proximal to the tube which was subsequently treated successfully with laser.

One patient presented with overgrowth at both ends of the tube 18 weeks after insertion of an Atkinson tube which had allowed her to swallow semi-solids. She had relatively little tumour at the distal end and the main overgrowth was at the top. The tumour proximal to the tube was successfully treated on 4 occasions by laser over a period of 17 weeks during most of which time she managed a semi-solid diet. She then developed an extrinsic stricture which could not be safely treated with laser. This was dilated and a short (9cm) Celestin tube was placed with its bottom end impacted into the funnel at the top of the Atkinson tube. Her swallowing was satisfactory in that she managed a semisolid diet but this did not represent any improvement on her swallowing prior to referral with overgrowth. She died 6 weeks after the second tube was inserted.

In all only 4 patients of the 14 studied were able to swallow fluids or better before treatment, the rest could swallow nothing (thus median dysphagia grade at presentation was 4). All patients except one benefited from improvement in swallowing of at least one dysphagia grade following treatment and ten patients by 2 clear grades. The median dysphagia grade for the survival period for each patient was calculated as in our previous study (Loizou 1991), and this ranged from 0-3 (the median for the series was 2). The improvement in dysphagia is significant at the 1% level using the Wilcoxon signed rank test and was achieved with only 1 or 2 endoscopies in 8 patients although, in the others, up to a maximum of 5 procedures were required. A median of one endoscopy was required for each 4 weeks survival. The median survival period was 9 weeks (range 3-36 weeks). The cause of death was cancer cachexia in most patients (11/14). A further 2 patients suffered with recurrent aspiration in addition to cancer cachexia which contributed to the cause of death. One of these had a chord paresis. One patient died of a myocardial Infarction and was swallowing well. Total hospital stay for endoscopic treatment ranged from 3-17 days (median 5 days) although several patients were hospitalised for longer for social reasons or transferred for hospice care. No perforations or other serious complications were encountered.

### 9.4 Discussion

Laser treatment with oesophageal prostheses in situ has been shown to be safe for most tubes. Moussin-Barbin tubes can however ignite and if laser treatment is essential we would recommend carbon dioxide to cool the fibre tip when treating patients with these tubes (Carter 1988). We have treated several patients with such tubes which have become displaced and to date have had no problems. Atkinson and Celestin tubes do not ignite and it is quite safe to use air for cooling in patients with such tubes in situ.

Ethanol induced tumour necrosis has been used to good effect in palliation of inoperable oesophageal cancer (Payne-James 1990) and other thermal methods such as the bipolar probe are also effective although it is only recommended for circumferential tumours (Jensen 1988). These techniques may also be useful for overgrowth although we do not have experience with them. The main advantage of laser is the ability to vaporise tissue resulting in an immediate improvement in the lumen which in turn allows instant access to and thus treatment of tumour beyond the area first treated. This results in an immediate improvement in swallowing. It is likely that the other techniques mentioned would also be effective in this group of patients but swallowing may only improve slowly as necrosed tissue takes a few days to slough. More treatment sessions may also be required to achieve the same result. We would therefore advocate the use of an Nd YAG laser if available.

It is only recently that we have been courageous enough to attempt tube manipulation after laser treatment. Shifting tubes which have been in position for several months requires caution as perforation is a definite risk. It is not possible to be certain of the distance between the lower end of the tumour and the bottom of the tube and so there is always a risk of uncovering tumour at the bottom end of the tube which may be more difficult to laser.

We successfully shifted tubes in 4 patients who had short overgrown areas. Despite this we feel that tube manipulation is inappropriate for most of these patients. This is because the prognosis is such that laser alone will usually provide good palliation for most of their lives without the necessity for multiple treatments and without the potential risks of tube manipulation. Overgrown areas are usually too narrow to allow easy passage of the Atkinson inserter and even in patients where this is possible it is likely that tumour debulking with laser prior to manipulation will be appropriate to reduce the risk of perforation. Thus an attempt at tube manipulation will usually involve repeated procedures that are difficult to justify in most cases.

There was one patient who underwent tube manipulation who could potentially have benefited from insertion of a longer tube. He had an overgrowth at the bottom of the tube which was shifted down to reveal tumour at the top end which was treated with laser. He swallowed semi-solids after treatment.

Two of the patients in this series had tubes inserted surgically and sewn in. This would have made proximal shifting impossible (although some downward displacement can still occur). It is important that this information is available to the endoscopist treating tube overgrowth as an attempt to shift such a tube proximally could be disastrous. It is now only rarely necessary for tubes to be inserted surgically as endoscopic techniques and equipment continue to improve, but even if laparotomy is required surgeons should be requested not to fix tubes with sutures as this severely limits the endoscopic options if complications arise later.

These results confirm the safety of laser treatment in patients with tubes in situ and validate an 'aggressive' treatment approach in most of these patients. The majority of those presenting with tube overgrowth have been well palliated for surprisingly long periods and when the overgrown area is treated with laser the patients swallowing is usually as good as that prior to overgrowth (usually dysphagia grade 2). The overgrown segment is mostly a short (median length 3 cm in this series) proliferative narrowing which is easily amenable to laser treatment and these results are usually therefore achieved with 1 or 2 procedures which is acceptable for this patient group.

# CHAPTER 10

## SUMMARY AND DISCUSSION

### 10.1 Palliation of oesophageal cancer

Accepting that Nd YAG laser presently offers an excellent treatment for palliation of oesophageal cancer we set out to assess the effect of additional external beam radiotherapy. There is a sound theoretical basis for the combination as outlined in chapter 2. However there was very little data available on the combination of laser and radiotherapy prior to these studies. A pilot study was performed initially in order to determine an appropriate radiotherapy dose regime, to assess if the combination treatment was promising and if so to provide data to allow us to estimate adequate numbers for a randomised study. The results of the pilot study were encouraging both in terms of reduced number of therapeutic procedures and possibly improved survival. The problem with a pilot study of this nature is that patients with better prognostic factors tend to be selected. Although these patients required markedly less frequent endoscopic procedures than historical controls treated with laser alone this may have been partly because the populations were different in the first place and not solely due to differences in treatment.

The subsequent randomised study confirmed that the period between therapeutic endoscopic procedures required to control dysphagia was prolonged in patients receiving external beam radiotherapy. The difference is not as great as the pilot study had suggested. The periods between therapeutic procedures required after 'check' endoscopy were increased to 9 weeks from 5 weeks which may be a useful benefit for some patients, particularly the minority who find endoscopic procedures very unpleasant or who have to travel long distances for treatment. There was however no difference in survival between those treated with laser only and laser with external beam radiotherapy. This is an important finding and casts doubt on the practice of giving external beam radiotherapy in the doses used to patients who are intubated for palliation of oesophageal cancer (Oliver 1990). A prolonged survival is the only conceivable benefit for such patients.

The use of endoluminal ultrasound in assessing tumour extent was useful. We demonstrated that external beam radiotherapy was probably having some effect on malignant nodes but the effect was not as great as that with chemotherapy. A reduction in node size in around 50% of similar cases treated with new chemotherapy regimes and monitored with CT scanning has been recorded (Mason 1992). Our results also showed that patients with bulky tumours or large involved nodes on endoluminal ultrasound have a poor prognosis and benefit little from this approach. Defining such patients who would not benefit from external beam radiotherapy is as important as defining those who will. To spare such patients the extra hospitalisation required for radiotherapy which encroaches on a limited prognosis is important.

We did not assess quality of life prior to laser. However the previous studies discussed do demonstrate quite an impressive improvement in scores after successful laser recanalisation. The quality of life assessments performed demonstrated a transitory fall during external beam radiotherapy. Overall there is no apparent long term difference between the two groups. It is reassuring that the more formal testing used correlates quite well with our own subjective impression of treatment outcome.

The positive correlation between the quality of life assessments used and quality of swallowing is highly significant but not strong. Overall only 18% of the variability in the QL index can be accounted for by the dysphagia grades recorded. This demonstrates that there are many other factors relevant to the quality of life. Such factors however may well be related to inexorable tumour growth and associated symptoms may be more difficult to control. Many patients who find their diagnosis difficult to accept may suffer an impaired quality of life purely due to the diagnosis of cancer. Dysphagia is however a symptom that can be directly addressed and relieving this troublesome symptom will improve quality of life irrespective of other factors. For maximum clinical benefit concentrating our efforts on attaining the best possible swallowing is therefore appropriate.

In future studies it would be interesting to correlate other factors with quality of life scores to determine more clearly which are important. One such factor often not directly assessed is nutrition. A period of a few weeks enteral nutrition either by nasogastric feeding tube or percutaneous endoscopic gastrostomy (PEG) after initial referral for palliation may improve quality of life.

It is also possible that frequent visits to hospital for laser treatment are beneficial as the care and attention provided by Nursing and Medical staff may lift the patients morale enough to improve quality of life scores. This would be more difficult to test in the clinical setting.

The cost data demonstrates a significant extra cost of £1150 for patients receiving radiotherapy. Overall the limited benefit from external beam radiotherapy is disappointing and the significant extra cost is difficult to justify. The finding that external beam radiotherapy is having some effect on the tumour is however important. It may be possible to improve on the radiotherapy effect with simpler and cheaper regimes.

Local radiotherapy (Brachytherapy) is becoming more practicable as more units have equipment such as the 'Selectron' which can deliver high dose rate sources to the relevant organ. Prior to this development such local treatment with a low dose rate source would have taken 2-3 days but can now be applied in 10 minutes. The operator only has to pass a nasogastric tube and programme the machine to deliver the dose required (usually 10Gy at a distance of 1 cm from the source) at the appropriate area. This approach delivers a high dose to the tumour but the dose rapidly falls off with distance from the source. Thus systemic effects should be minimal. There is however some doubt that large nodes will be adequately treated as they may be several centimetres from the source. This problem may be partly addressed by a second treatment after a few weeks.

Day case treatment with Brachytherapy costs no more than the equivalent of 2 or 3 days hospitalisation. If it is as effective as external beam treatment in reducing the necessity for further endoscopies the cost saving on follow up procedures equal the costs of brachytherapy. Early data from our unit in 15 patients with adenocarcinomas of the cardia (Spencer 1994) indicates that this approach may be more effective than external beam radiotherapy and further work is justified. Other promising approaches include shorter external beam radiotherapy regimes (Bleehan 1991) or combination of external beam radiotherapy and brachytherapy (Agrawal 1992).

### 10.2 Palliation of rectosigmoid cancer

The results of laser and radiotherapy for rectosigmoid cancer are more encouraging than those for oesophageal cancer with the reservation that only a small number of patients have been treated in a pilot study. The laser treatment intervals for effective palliation for this group appear to have increased from 1 month to about 3 months with the addition of external beam radiotherapy. In the context of an impressive median survival of 15 months these results are very promising. Most of the studies on laser as palliation for rectal cancer discussed in chapter 2 report median survival times of around 6 months and so this may represent a survival benefit. It is important to remember that the patients selected as suitable for this trial were only around 1/3 of allcommers and a larger randomised study needs to be performed to confirm these results.

### 10.3 Collaboration with radiotherapists

We have found that there is an important advantage in locating a laser in a unit associated with interested radiotherapy team. It allows a radiotherapy opinion to be obtained and treatment to be commenced promptly in appropriate patients. The expertise in counselling and support available from nurses trained in oncology may also be a benefit. Many patients with squamous cell oesophageal cancer are referred directly for radiotherapy. During the course of collaborative studies we have received more referrals of such patients from radiotherapists as they have become more aware how effective endoscopic techniques can be in restoring swallowing quickly. The availability of endoscopic expertise may thus prevent patients languishing on oncology wards unable to swallow and requiring NG feeding.

The cooperation between specialties works both ways. We have been treating groups of patients such as those with squamous cell oesophageal cancer and many of those with rectal cancers who would previously have been treated by radiotherapists. It is therefore not surprising that they also have expertise which we lack. A few patients with squamous cell oesophageal cancers referred to us for palliation have been deemed suitable for radical radiotherapy treatment. One of these patients is alive and disease free after more than 3 years! Another group often referred for laser are those with low rectal cancers growing into the perineum. Being superficial, the response to radiotherapy is good and usually superior to that possible with laser.

### 10.3 The laser and tube-a complimentary duo

Over the last few years there has been an ongoing debate on the relative merits of tube and laser. We would argue that they are complimentary; use of the appropriate modality at a given point in time for each individual will maximise benefit with the least number of interventions possible.

An earlier paper from our unit (Loizou 1991) described a prospective comparison of laser therapy and intubation in the palliation of malignant dysphagia. The results were discussed in detail in chapter 2. Overall the group receiving laser swallowed better than those intubated but required more procedures (mean 4.6 v 1.4). Solids could be managed for more than half the survival time in 1 in 3 of those treated with laser but only 1 in 10 of those intubated. In addition the proportion of patients managing fluids only is double in patients intubated compared with patients receiving laser therapy (19% v 8%). In simple terms around 1/3 of these patients swallowed better with laser than a tube but more than 70% of those intubated will manage at least semi-solids.

The dysphagia data as reported by Loizou gives a slightly pessimistic view as many laser treated patients managing a semi solid diet most of the time are able to eat some solids for a period after each treatment and are thus doing better than with a tube! Many such patients are reluctant to be intubated but are content to have repeated laser treatments. In the randomised study looking at laser and radiotherapy dysphagia results are rather better. Around two thirds of the patients entered swallowed some solids for most of their remaining lives. This may be partly due to patient selection as patients had to be considered fit for external beam radiotherapy. It is possible however that our technique is now more 'aggressive' than in the previous study. We are probably 'vaporising' more tumour than previously and this may account for some of the discrepancy. Reviewing the recent literature there is some evidence to suggest that well over half of those treated with the Nd YAG laser do indeed manage a solid diet for much of their survival (Naveau 1990, Mason 1991).

Most studies discussed in chapter 2 report a far higher complication rate with intubation than with laser. One can therefore argue that many of those managing semi-solids on average with laser should not be intubated and our policy is to carefully assess each patient individually.

The management of patients who are unable to manage semi-solids most of the time with laser or whose survival is likely to be short is less controversial. We routinely advise such patients to be intubated.

Expanding further on the same theme there are situations where tubes can benefit patients with laser and radiotherapy induced complications. Chapter 8 describes the use of cuffed (Wilson Cooke) tubes in 3 groups of patients with complications some of which were laser induced. These tubes are designed for patients with malignant oesophago-respiratory fistulae. We have treated seven such cases 2 of whom had laser induced fistulae. Six closed after intubation and the other tube displaced and could not be repositioned. Patients with instrumental perforation and those with life threatening arterial bleeding from cardia cancers in whom laser was ineffective also benefited from these tubes.

Chapter 9 documents the successful use of Nd YAG laser in 14 patients with overgrowth of conventional tubes; this is another example of optimising patient benefit by using the appropriate treatment modality at the right time.

In summary we argue that laser and tube are complimentary. The availability of both treatments offers any individual a better initial choice than either alone and should he or she develop complications later on the option of resorting to the "other" modality may be advantageous.

The tube studies performed confirm that tubes and laser are complimentary treatments in patients with oesophageal cancer. It is therefore important that centres performing endoscopic treatment should be equiped for a variety of treatments. X-ray screening is necessary for tube insertion. Such facilities are more likely to be available in specialist centres.

## 10.4 The future

In order to improve further on the results for cancers it is likely that combination treatments will be required. What is needed is a technique for rapid and prolonged restoration of the lumen. Options of new radiotherapy regimes have already been discussed. Hopefully such approaches may also improve survival. Certainly this seems possible for patients with rectal cancer. Other techniques for recanalisation may be enhanced by a combination approach. The most promising of these is alcohol injection (Payne -James 1991). Such techniques however will never have the precision of laser. The other practical advantage of laser is the ability to vaporise tumour allowing immediate improvement in swallowing and early discharge from hospital.

The use of endoluminal ultrasound to monitor response to therapy probably represents an improvement over CT scanning. This technique, with the Aloaka probe used by us, is relatively cheap, quick and easy and needs to be used to assess new treatment combinations and modalities. The Aloaka probe used is particularly well suited to monitoring local tumour response as local nodes are seen clearly. The lower frequency (5Mz) results in a less detailed near image so that the 5 layer oesophageal wall structure cannot be identified. This is however unimportant in patients undergoing laser as oesophageal wall images are difficult to interpret in any case. This technique is likely to prove increasingly useful in monitoring the effect of new treatments (such as chemotherapy {Mason 1991}) used in combination with laser.

A promising new laser technique for patients with early cancers is that of Photodynamic therapy. The tumour is sensitised with a chemical which releases singlet oxygen when excited by laser light at an appropriate wavelength in the presence of oxygen. Such an approach looks hopeful in patients with gastrointestinal lesions (Barr 1990b, Regula 1993). There are still however some technical problems and very few patients present with early lesions suitable for such treatment.

An interesting development which may have important therapeutic implications is the use of metallic stents. A recent series (Diego 1993) of 64 patients with oesophageal cancer demonstrated good palliation with complication rate much lower than conventional tubes. This study did not document dysphagia in detail but as the stents expand to 18mm it is likely that swallowing is excellent. Use of these stents is only recommended in patients who have an open oesophagus after dilatation. Many patients do not fall into this category and laser recanalisation may be required. Use of intraluminal or external beam radiotherapy after stenting in an attempt to prolong survival would be an option. The stent would hopefully prevent the development of radiation strictures perhaps allowing larger doses to be safely applied. It is possible that such an approach (with a larger diameter stent) may also be possible with rectal cancers.

Endoscopic Nd YAG laser therapy now has a well established role in specialist centres which have an interest in therapeutic endoscopy. It is highly effective at relieving dysphagia when used alone. New developments in combination therapy may continue to improve results in at least some patient groups who presently benefit from such therapy.

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# APPENDIX 1

Oesophageal pilot study raw data

| No | age | sex | site | L | hist | mets | IP | dg 1 | dg2 | dg3 | dg4 | DXRT | LT init | LT post RT | FO RX What | sur | CK IST RPT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 50 | M | C | 13 | A | Y | 28 | 3.0 | 3.0 | 3.0 | 3.0 | 30/10 | 5 | 1 | L | 9 | 2 TO DTH |
| 2 | 73 | M | C | 11 | A | N | 8 | 2.0 | 1.0 | 3.5 | 3.5 | 40/20 | 2 | 0 | | 14 | 8 TO DTH |
| 3 | 68 | M | C | 6 | A | N | 27 | 2.0 | 2.0 | 2.0 | 2.0 | 30/10 | 2 | 1 | L D | 15 | 9 TO DTH |
| 4 | 85 | M | C | 4 | A | N | 21 | 2.0 | 1.0 | 0.5 | 0.5 | 30/10 | 2 | 0 | | 20 | 14 TO DTH |
| 5 | 69 | M | C | 10 | A | N | 25 | 2.0 | 1.0 | 1.0 | 1 | 30/10 | 2 | 0 | D | 25 | 9 TO DTH |
| 6 | 74 | F | C | 12 | A | N | 31 | 3.0 | 2.0 | 0.5 | 2.0 | 30/10 | 3 | 4 | L+I | 27 | 5 |
| 7 | 69 | M | C | 3 | A | N | 28 | 2.5 | 1.0 | 0.0 | 1.0 | 40/10 | 2 | 1 | L D | 50 | 9 |
| 8 | 65 | M | A | 4 | A | N | 31 | 2.5 | 1.0 | 1.0 | 1.0 | 30/10 | 6 | 6 | L D | 51 | 4 |
| 9 | 77 | M | C | 7 | A | N | 14 | 1.5 | 1.0 | 0.0 | 1.0 | 30/15 | 1 | 3 | L D | 61 | 12 |
| 10 | 55 | M | C | 10 | A | Y | 10 | 1.5 | 0.0 | 0.0 | 0.0 | 30/10 | 3 | 2 | L | 66 | 24 |
| 11 | 66 | M | C | 4 | A | Y | 40 | 3.0 | 3.0 | 3.0 | 3.0 | 40/15 | 3 | 0 | I AT 37/52 | 73 | 26 |
| 12 | 68 | M | C | 7 | A | N | 24 | 4.0 | 0.0 | 0.0 | 0.5 | 30/10 | 5 | 5 | LT | 83 | 23 |
| 13 | 61 | F | C | 9 | A | N | 24 | 2.0 | 0.0 | 0.0 | 1.0 | 30/10 | 2 | 4 | L | 105 | 7 |
| 14 | 47 | M | C | 10 | S | Y | 19 | 3.0 | 2.0 | 3.5 | 3.5 | 40/10 | 3 | 2 | L | 7 | 1 TO DTH |
| 15 | 76 | F | UT | 5 | S | N | 35 | 4.0 | 3.0 | 3.0 | 3.0 | 30/10 | 4 | 0 | | 8 | 3 TO DTH |
| 16 | 64 | M | C | 8 | S | Y | 30 | 2.0 | 1.0 | 0.5 | 0.5 | 40/20 | 2 | 1 | L | 8 | 1 TO DTH |
| 17 | 80 | F | UT | 3 | S | N | 16 | 3.0 | 2.0 | 1.0 | 0 | 20/10 | 1 | 0 | | 24 | 19 TO DTH |
| 18 | 55 | M | C | 5 | S | Y | 25 | 3.0 | 1.5 | 3.5 | 2.5 | 40/10 | 3 | 2 | L D | 24 | 4 |
| 19 | 81 | M | LT | 6 | S | N | 20 | 2.0 | 1.0 | 0.0 | 0.0 | 30/10 | 2 | 1 | L | 38 | 34 TO DTH |
| 20 | 46 | F | UT | 5 | S | N | 21 | 2.5 | 1.0 | 0.5 | 0.5 | 30/10 | 2 | 1 | L | 47 | 22 |
| 21 | 78 | F | LT | 6 | S | N | 6 | 2.0 | 1.5 | 0.0 | 0.5 | 30/10 | 2 | 0 | D | 78 | 17 |
| 22 | 78 | F | UT | 3 | S | N | 18 | 2.5 | 1.0 | 0.0 | 0.0 | 30/10 | 2 | 0 | D | 147 | 132+ |

# APPENDIX 1 Column key

| | |
|---|---|
| Age | (years) |
| Site | C=Cardia UT=Upper thoracic LT=Lower thoracic A=Anastomotic |
| L | Length in centimetres |
| Hist | Histology : A=Adenocarcinoma S=Squamous cell cancer |
| Mets | Metastases |
| I P | In patient treatment time in days |
| DG 1 | Dysphagia grade at presentation |
| DG 2 | Dysphagia grade after initial laser course |
| DG 3 | Dysphagia grade after radiotherapy course |
| DG 4 | Mean dysphagia grade after radiotherapy |
| DXRT | Radiotherapy regime Gy/fractions |
| LT init | Initial number of laser treatments for recanalisation |
| LT post RT | Number of laser treatments after radiotherapy |
| Fo Rx what | What follow up treatment ? L=Laser D=Dilatation I=Intubation |
| Surv | Survival in weeks |
| CK 1ST RPT | Time in weeks from 'check' endoscopy to first repeat |
| TO DTH | No 'check' endoscopy prior to death |

# APPENDIX 2

## Oesophageal randomised study raw data

| NO | AGE | SEX | SITE | L | HIST | METS | WHY LASER | IP | DG1 | DG2 | DG3 | DG4 | RT | LT INI | CK | LES CK | LES PO CK | RXS PC | RX POST CK | TIME CK TO FU | WKS PROC | DEAD? | SURVIV | CK 1ST RPT |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 75 | F | C | 3 | A | N | AGE MED | 36 | 3 | 2 | 2 | 2 | Y | 2 | D 2L | REC T | REC T | 4 | 2 LT | 60 | 20 | D | 76/52 | 48/52 |
| 2 | 65 | M | C | 6 | A | Y | METS | 0 | 1 | 1 | 2 | 2 | N | 2 | 0 | GL | REC T | 1 | 1 | 5 | 3 | D | 6/52 | 4/52 |
| 3 | 66 | F | C | 6 | A | N | MED | 42 | 3 | 2 | 1 | 1 | Y | 3 | D | S | REC T S | 9 | 6L 2D T | 52 | 7 | D | 98/52 | 13/52 |
| 4 | 74 | M | C | 6 | A | N | AGE MED | 9 | 3 | 1 | 1 | 1 | N | 3 | 2L | REC T | REC T | 1 | L | 11 | 6 | D | 17/52 | 5/52 |
| 5 | 80 | M | C | 4 | A | N | AGE MED | 32 | 4 | 1 | 0 | 0 | Y | 3 | L | REC T | | 0 | 0 | 13 | 13 | D | 19/52 | 13/52 TO DTH |
| 6 | 67 | M | ANA | 7 | A | N | ANA | 13 | 4 | 1 | 0 | 1 | Y | 3 | L | REC T | REC T | 2 | LT | 9 | 9 | D | 18/52 | 9/52 |
| 7 | 75 | M | C | 3 | A | N | EXT(LAP) | 20 | 2 | 1 | 1 | 1 | N | 5 | LD | REC T | REC T | 7 | 4L T TM | 9 | 4 | D | 40/52 | 4/52 |
| 8 | 84 | M | C | 8 | A | N | EXT AGE | 53 | 2 | 1 | 2 | 2 | Y | 4 | 0 | GL | REC T | 6 | 4L T | 17 | 5 | D | 35/52 | 9/52 |
| 9 | 81 | M | C | 10 | A | N | AGE MED | 23 | 2 | 0 | 1 | 1 | N | 4 | 2L | REC T | REC T | 2 | 2L | 26 | 9 | D | 31/52 | 5/52 |
| 10 | 66 | M | C | 6 | A | Y | METS | 16 | 2 | 0 | 1 | ? | Y | 4 | L | REC T | | 0 | 0 | 4 | 4 TO DTH | D | 12/52 | 4/52 TO DTH |
| 11 | 60 | M | C | 4 | A | N | EXT (LAP) | 21 | 3 | 0 | 2 | 2 | N | 4 | D | GL | S | 6 | 3D T TM | 9 | 3 | D | 22/52 | 6/52 |
| 12 | 81 | F | C | 3 | A | N | AGE MED | 23 | 3 | 1 | 3 | 1 | N | 4 | 2L | T | S | 2 | T | 5 | 5 | D | 35/52 | 5/52 |
| 13 | 85 | F | C | 6 | A | N | AGE MED | 22 | 2 | 1 | 2 | 2 | Y | 2 | L | REC T | S | 1 | T | 3 | 3 | D | 9/52 | 3/52 |
| 14 | 67 | M | ANA | 4 | A | N | MED | 5 | 2 | 0 | 0 | 0 | N | 3 | O | | | | | | NA | D | 7/52 | NO CK |
| 15 | 79 | M | C | 5 | A | N | AGE EXT | 42 | 3 | 1 | 0 | 1 | Y | 7 | 0 | NEC T GL | S REC T | 4 | 2 DL 2L | 41 | 10 | D | 70/52 | 9/52 |
| 16 | 58 | M | C | 7 | A | N | MED | 33 | 3 | 1 | 1 | 1 | Y | 3 | DL | S T | S T | 1 | D T | 9 | 5 | D | 15/52 | 8/52 |
| 17 | 64 | M | C | 7 | A | Y | METS | 37 | 4 | 1 | 2 | 3 | Y | 3 | 0 | 0 | | 0 | 0 | 3 | 3 TO DTH | D | 9/52 | 3/52 TO DTH |
| 18 | 58 | M | ANA | 8 | A | N | ANA | 15 | 2 | 2 | 2 | | N | 2 | 3L | REC T | REC T | 3 | 2L T at 9/52 | 9 | 3 | D | 47/52 | 2/52 |
| 19 | 74 | M | C | 12 | A | N | AGE MED | 9 | 3 | 1 | 2 | | Y | 2 | 0 | | | 0 | 0 | | NA | D | 3/52 | NO CK |
| 20 | 67 | F | ANA | 6 | A | N | EXT (CT) | 28 | 4 | 2 | 2 | 2 | N | 3 | 2L | REC T | REC T | 2 | 2L | 12 | 6 | D | 18/52 | 9/52 |
| 21 | 82 | M | C | 12 | A | N | AGE MED | 7 | 2 | 1 | 1 | 2 | Y | 2 | 0 | | - | 0 | 0 | | NA | D | 11/52 | NO CK |
| 22 | 66 | M | C | 5 | A | N | MED | 8 | 2 | 1 | 0 | | N | 3 | - | - | - | 0 | 0 | | NA | D | 6/52 | NO CK |
| 23 | 72 | M | C | 14 | A | N | EXT (CT) | 24 | 2 | 1 | 0 | 1 | Y | 4 | 0 | NONE | REC T S | 2 | LD L | 15 | 7 | D | 22/52 | 7/52 |
| 24 | 70 | M | ANA | 16 | A | N | AGE MED | 25 | 2 | 1 | 1 | 2 | N | 3 | D | S | REC T S | 6 | LD 2L D DT | 28 | 6 | D | 44/52 | 7/52 |
| 25 | 76 | M | LT | 6 | A | N | MED EXT | 34 | 2 | 1 | 1 | 1 | Y | 2 | D | S | S | 2 | 4D L LT | 32 | 5 | D | 51/52 | 6/52 |
| 26 | 75 | M | C | 10 | A | Y | MED | 9 | 1 | 0 | 0 | 1 | N | 4 | L | REC T | REC T | 1 | L | 28 | 14 | D | 34/52 | 9/52 |
| 27 | 69 | M | C | 16 | A | N | EXT | 8 | 3 | 2 | 2 | 2 | Y | 4 | NO CK | | | 0 | 0 | | NA | D | 8/52 | NO CK |
| 28 | 63 | M | C | 11 | A | Y | METS | 18 | 2 | 1 | 1 | 1 | Y | 2 | - | | 0 | 0 | - | | NA | D | 5/52 | NO CK |
| 29 | 78 | M | C | 12 | A | Y | METS | 14 | 3 | 0 | 0 | 1 | N | 4 | 2L | REC T | REC T | 1 | T | 15 | 15 | D | 33/52 | 15/52 |
| 30 | 60 | M | C | 6 | A | Y | METS | 9 | 4 | 1 | | | N | 5 | 2 LD | REC T S | 0 | | | | NA | D | 10/52 | TUBE AT CK |
| 31 | 66 | M | C | 12 | A | Y | METS | 13 | 3 | 1 | 1 | 2 | N | 2 | L | REC T | REC T S | 4 | DL D L L | 22 | 6 | D | 25/52 | 4/52 |
| 32 | 64 | M | C | 9 | A | N | EXT (CT) MED | 17 | 3 | 1 | 2 | | N | 2 | 2L | | REC T | 1 | L | | 2 TO DTH | D | 7/52 | 2/52 TO DTH BL |
| 33 | 74 | M | C | 10 | A | N | EXT | 4 | 3 | 0 | 0 | 1 | Y | 2 | L | REC T | REC T | 5 | 5L | 39 | 10 | D | 48/52 | 9/52 |
| 34 | 74 | M | C | 7 | A | N | MED AGE | 23 | 3 | 2 | 2 | 2 | N | 1 | 2L | REC T | REC T | 10 | 10 L | 39 | 4 | D | 49/52 | 6/52 |
| 35 | 65 | M | C | 5 | A | Y | METS | 3 | 2 | 0 | 0 | 0 | Y | 2 | L | REC T | | 0 | 0 | 11 | 11 TO DTH | D | 20/52 | 10/52 TO DTH |
| 36 | 73 | M | C | 4 | A | Y | METS | 4 | 4 | 2 | 1 | 1 | N | 2 | DL L | REC T | | 0 | 0 | 2 | 2 | D | 9/52 | 2/52 TO DTH |
| 37 | 50 | M | ANA | 2 | A | N | ANA | 21 | 2 | 1 | 1 | 1 | Y | 2 | L | REC T | S S T | 3 | 2D LD | 14 | 5 | D | 20/52 | 7/52 |
| 38 | 66 | M | ANA | 5 | A | N | ANA | 4 | 1 | 1 | 1 | 2 | Y | 2 | | | | 0 | | | NA | D | 4/52 | NO CK |
| 39 | 73 | M | C | 5 | A | N | MED | 14 | 2 | 1 | 2 | | Y | 1 | 0 | GL | | 0 | | 6 | 6 | D | 14/52 | 6/52 |
| 40 | 59 | M | ANA | 4 | A | N | EXT | 6 | 2 | 1 | 1 | 1 | Y | 2 | D | S | | 0 | | 23 | 23 | D | 28/92 | 23/52 TO DTH |
| 41 | 72 | M | LT | 8 | S | N | AGE MED | 29 | 3 | 0 | 0 | 2 | Y | 3 | D | S | REC T | 8 | 8 L T | 22 | 4 | D | 30/52 | 11/52 |
| 42 | 85 | M | C | 8 | S | N | AGE | 5 | 3 | 1 | 1 | 1 | N | 3 | D | S | | | | | NA | D | 8/52 | NO CK |
| 43 | 83 | F | LT | 3 | S | N | AGE MED | 12 | 2 | 1 | 2 | 2 | N | 3 | LD | S | REC T | 2 | D T | 9 | 9 | D | 25/52 | 9/52 |
| 44 | 61 | F | LT | 11 | S | N | MED | 23 | 3 | 1 | 2 | 2 | N | 6 | T | REC T | | | | | 0 | D | 21/52 | 0/52 |
| 45 | 57 | M | C | 5 | S | Y | METS | 7 | 3 | 1 | 1 | 1 | Y | 3 | L | REC T | | 0 | 0 | 12 | 12 | D | 17/52 | 12/52 TO DTH |
| 46 | 88 | F | LT | 10 | S | N | AGE MED | 27 | 3 | 1 | 1 | 1 | N | 3 | 2L | REC T | REC T S | 8 | 8LD | 52 | 7 | D | 57/52 | 6/52 |
| 47 | 73 | F | LT | 7 | S | N | AGE MED | 23 | 3 | 1 | 0 | 1.0 | Y | 3 | D | S | S T | 2 | L T | 27 | 13 | D | 34/52 | 19/52 |
| 48 | 77 | F | C | 6 | S | N | AGE MED | 12 | 3 | 1 | 1 | 2 | Y | 2 | D | S | S T | 1 | DL | 25 | 25 | D | 33/52 | 5/52 |
| 49 | 78 | M | LT | 6 | S | N | AGE MED | 24 | 4 | 1 | 2 | 2 | N | 5 | 2L | S T | S T | 3 | DL 2L | 12 | 12 | D | 20/52 | 10/52 |
| 50 | 70 | M | C | | S | N | EXT | 20 | 4 | 1 | 2 | 2 | Y | 7 | D | ST | | 2 | D | 19 | 10 | D | 29/52 | 6/52 |
| 51 | 75 | M | C | 8 | S | N | MED | 29 | 3 | 1 | 2 | 2 | Y | G | D | S | S | 3 | 3D | 34 | 11 | D | 34/52 | 6/52 |
| 52 | 71 | F | LT | 9 | S | N | EXT (CT) | 11 | 2 | 1 | 0 | 1 | Y | 3 | D | S | S | 2 | D | 14 | 7 | D | 29/52 | 8/52 |
| 53 | 70 | F | LT | 4 | S | N | MED | 34 | 3 | 2 | 2 | 2 | Y | 3 | 2 DL | REC T S | S | 4 | 2D DT TC TM | 13 | 4 | D | 23/52 | 9/52 |
| 54 | 65 | M | LT | 10 | S | N | MED | 9 | 2 | 1 | 0 | | N | 2 | L | REC T | - | 0 | 0 | 6 | 6 TO DTH | D | 15/52 | 6/52 TO DTH |
| 55 | 73 | F | LT | 10 | S | N | AGE MED | 6 | 4 | 2 | 2 | 2 | N | 4 | L | REC T | REC T | 3 | 2L T | 9 | 3 | D | 24/52 | 5/52 |
| 56 | 68 | M | LT | 9 | S | Y | METS | 9 | 3 | 1 | 1 | 1 | Y | 2 | DL | S REC T | S | 4 | 3D T | 40 | 10 | D | 54/52 | 11/52 |
| 57 | 56 | M | UT | 7 | S | Y | METS | 13 | 2 | 1 | 1 | 1 | N | 2 | 2 D L | S REC T | REC T | 7 | 3L D T TM | 19 | 5 | D | 54/52 | 5/52 |
| 58 | 69 | F | C | 10 | S | Y | METS | 18 | 4 | 1 | 1 | 1 | N | 3 | DL | S REC T | REC T S | 4 | 2L LD D | 28 | 6 | D | 34/52 | 3/52 |
| 59 | 77 | F | UT | 5 | S | N | AGE MED | 11 | 2 | 2 | 2 | 2 | N | 2 | DT | S | - | O | 0 | 26 | T at CK | D | 30/52 | 0 |
| 60 | 78 | F | LT | 2 | S | N | MED REF SURG | 20 | 2 | 1 | 1 | 1 | Y | 2 | L | REC T | REC T S | 1 | - | 10 | 12 | D | 31/52 | 10/52 |
| 61 | 67 | M | LT | 4 | S | N | MED | 21 | 3 | 2 | 1 | 0 | Y | 3 | 2D | S | 0 | 0 | 0 | 23 | 23 | D | 30/52 | 23/52 |
| 62 | 82 | F | LT | 4 | S | N | MED AGE | 14 | 3 | 2 | 1 | 2 | Y | 2 | D | S | | 0 | 0 | 0 | 0 | D | 9/52 | TUBE AT CK |
| 63 | 67 | F | UT | 8 | S | N | MED AGE | 14 | 3 | 2 | 1 | 1 | N | 1 | D L | S REC T | S REC T | 4 | LD L D T | 61 | 7.5 | D | 65/52 | 6/52 |
| 64 | 84 | F | C | 4 | S | N | AGE MED | 19 | 4 | 2 | 1 | 1 | Y | 2 | D | S | S | 2 | D T | 17 | 9 | D | 25/52 | 10/52 |
| 65 | 78 | F | LT | 6 | S | N | AGE MED | 13 | 3 | 3 | 3 | | Y | 3 | D | S | 0 | 0 | 0 | | 0 | D | 4/52 | 0 |
| 66 | 67 | M | UT | 8 | S | N | AGE MED | 13 | 1 | 0 | 1 | 2 | Y | 2 | D | | S | 3 | D DL DT | 31 | 8 | D | 63/52 | 7/52 |
| 67 | 78 | F | UT | 6 | S | N | AGE MED | 16 | 1 | 1 | 1 | 2 | N | 3 | L | REC T | REC T | 3 | 2D | 28 | 7 | D | 34/52 | 4/52 |

# APPENDIX 2 Column key

See appendix 1 also........

| | |
|---|---|
| Why laser | Reason for laser treatment. EXT=tumour extent MED=general medical disease AGE=Old age |
| CK | Treatment at 'check' endoscopy D=Dilatation, L=Laser, T=Tube |
| LES CK | Lesion at 'check' endoscopy REC T=Recurrent tumour S=Stricture GL=Good lumen |
| LES po CK | Lesion at later procedures. Key as 'Les CK' |
| RXS PC | Number of procedures after 'check' endoscopy |
| RX POST CK | Treatment after 'check' endoscopy L=Laser D=Dilatation T=Tube TM=Tube manipulation TC=Tube change |
| TIME | Follow up time from 'check' endoscopy onwards |
| WKS PROC | Number of weeks between each procedure after 'check' endoscopy |

# APPENDIX 3

oesophageal ultrasound data

| N' | SEX | L | METS | RT | PRE RT US | RX US | US1 T | US1 N | US 2 DATE | RX US 2 | US 2 T | US2 N |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | M | 6 | Y | N | 9/90 | 0 | 2 | 2/2 | | | | |
| 3 | F | 6 | N | Y | 16/90 | 0 | 10 | 1/7 | 23/90 | 0 | 10 | 3/9 |
| 4 | M | 6 | N | N | 15/90 | 0 | 1.5 | 1/1 | 20/90 | 0 | 1.6 | 2/0.8 |
| 5 | M | 4 | N | Y | 19/90 | 0 | 1.8 | 1/2 | 24/90 | 6000 | 2.1 | |
| 6 | M | 7 | N | Y | 19/90 | 0 | 2.1 | | 24/90 | 6000 | 1.5 | 2/1.4 |
| 7 | M | 3 | N | N | 28/90 | 19000 | 1.4 | 1/0.5 | | | | |
| 8 | M | 8 | N | Y | 32/90 | 0 | 1.6 | 2/1.4 | 36/90 | 0 | 3.2 | 1/1.2 |
| 9 | M | 10 | N | N | 32/90 | 22000 | 3.2 | 1/1.3 | 32/90 | 5000 | 1.4 | |
| 10 | M | 6 | Y | Y | 32/90 | 19000 | 1.8 | 1/2.4 | 43/90 | 15000 | 1.2 | 1/1.5 |
| 11 | M | 4 | N | N | 33/90 | 0 | 1.3 | 1/1.3 | 38/90 | D | 1.3 | 1/1.3 |
| 12 | F | 3 | N | N | 37/90 | 0 | 1.3 | 2/0.9 | 43/90 | 0 | 3 | 1/0.6 |
| 13 | F | 6 | N | Y | 37/90 | D | 2.4 | 1/1.0 | 42/90 | 4000 | 2.7 | 2/2.0 |
| 14 | M | 4 | N | N | 42/90 | 6000 | 4.8 | 2/0.8 | | | | |
| 15 | M | 5 | N | Y | 50/90 | 0 | 1.6 | | 5/91 | 0 | 3 | 1/0.5 |
| 16 | M | 7 | N | Y | 1/91 | 3000 | 0.8 | | 6/91 | 15000 | 1.3 | |
| 17 | M | 7 | Y | Y | 51/90 | L | 2.1 | 1/0.8 | 4/91 | 0 | 1.9 | |
| 18 | M | 8 | N | N | 6/91 | 28000 | 1.5 | 1/1 | 12/91 | 0 | 1.9 | 1/1 |
| 19 | M | 12 | N | Y | 6/91 | 31000 | 2.2 | 4/1.4 | | | | |
| 21 | M | 12 | N | Y | 10/91 | 1200 | 1.8 | 3/2.2 | | | | |
| 23 | M | 14 | N | Y | 14/91 | 11000 | 2 | 3/1.2 | 19/91 | 0 | 1.6 | 3/0.5 |
| 24 | M | 16 | N | N | 14/91 | 4000 | 1.0 | 1.3 | 27/91 | 0 | 1.2 | 1.5 |
| 25 | M | 6 | N | Y | 14/91 | 7000 | 2.0 | 5/1.9 | 20/91 | D | 1.2 | 3/2.1 |
| 26 | M | 10 | Y | N | 17/91 | 10000 | 3.4 | 2/0.5 | 23/91 | 13000 | 2.6 | 8/1.0 |
| 27 | M | 16 | N | Y | 18/91 | 8000 | 2 | 3/2.6 | | | | |
| 28 | M | 11 | Y | Y | 17/91 | 17000 | 1.6 | 8/1.3 | | | | |
| 29 | M | 12 | Y | N | 19/91 | 9000 | 4.2 | - | 29/91 | 10000 | 1.8 | - |
| 30 | M | 6 | Y | N | 20/91 | 9000 | 0.9 | 2/2.5 | | | | |
| 31 | M | 12 | Y | N | 19/91 | 9000 | 1.6 | 2/0.9 | | | | |
| 33 | M | 10 | N | Y | 19/91 | 12000 | 1.3 | 3/2.4 | 33/91 | 5000 | 1.8 | 3/2.3 |
| 34 | M | 7 | N | N | 25/91 | 0 | 1.2 | 2/0.7 | 30/91 | 9000 | 3.2 | |
| 35 | M | 5 | Y | Y | 28/91 | 9000 | 1.7 | 2/0.8 | 36/91 | 4500 | 2 | 2/0.7 |
| 36 | M | 4 | Y | N | 30/91 | 0 | 2.3 | 4/1.9 | 35/91 | 8000 | 2.5 | 3/1.6 |
| 37 | M | 2 | N | Y | 32/91 | 4000 | 1.3 | 3/1.4 | | | | |
| 39 | M | 5 | N | Y | 44/91 | 0 | 1.3 | | 50/91 | 0 | 2.5 | |
| 40 | M | 4 | N | Y | 48/91 | 0 | 1.0 | | 2/92 | 0 | 0.6 | |
| 42 | M | 8 | N | N | 15/90 | D | 2.1 | 3/1.6 | 19/90 | D | 2.2 | 1/1.6 |
| 43 | F | 3 | N | N | 30/90 | D | 1.1 | | 35/90 | D | 1.5 | |
| 44 | F | 11 | N | N | 32/90 | 0 | 1.5 | 1/2.1 | | | | |
| 46 | F | 10 | N | N | 36/90 | 7000 | 1.4 | | 43/90 | 16000 | 2.3 | |
| 47 | F | 7 | N | Y | 41/90 | 0 | 1 | 1/0.7 | 47/90 | D | 1.9 | 1/1.4 |
| 48 | F | 6 | N | Y | 42/90 | 10,000 | 0.9 | | 50/90 | D | 1.3 | 1/0.7 |
| 49 | M | 6 | N | N | 48/90 | 4000 | 3.3 | 5/1.6 | 1/91 | 12000 | 2 | 6/1.4 |
| 50 | M | | N | Y | 19/91 | 13,000 | 2.8 | 1.0 | | | | |
| 52 | F | 9 | N | Y | 27/91 | 9000 | 1.7 | 2/2.3 | 33/91 | 1000 | 1.1 | |
| 53 | F | 4 | N | Y | 27/91 | 7000 | 0.9 | | 34/91 | 2500 | 1.7 | 2/1.6 |
| 54 | M | 10 | N | N | 32/91 | 15000 | 1.6 | 2/1.3 | 36/91 | 9000 | 1.5 | 1/1.8 |
| 55 | F | 10 | N | N | 33/91 | 9000 | 2.4 | 2/0.9 | 39/91 | 7000 | 1.0 | 1/1.7 |
| 56 | M | 9 | Y | Y | 34/91 | 6000 | 2.3 | 3/1.2 | 47/91 | 3000 | 1.1 | 2/0.6 |
| 57 | M | 7 | Y | N | 39/91 | 6000 | 1.3 | 0 | 43/91 | 4000 | 1.7 | 1.1 |
| 58 | F | 10 | Y | N | 46/91 | 3000 | 3 | 3/2.2 | | | | |
| 59 | F | 5 | N | N | 47/91 | 5000 | 1 | 1/1.0 | 2/92 | 3000 | 1.3 | 2/1.7 |
| 60 | F | 2 | N | Y | 6/92 | 0 | 1.3 | | | | | |
| 61 | M | 4 | N | Y | 6/92 | 0 | 1 | | 11/92 | D | 1.4 | 1/0.6 |
| 62 | F | 4 | N | Y | 11/92 | 0 | 1.2 | | | | | |
| 63 | F | 8 | N | N | 13/92 | O | 1.0 | 2/1.7 | 17/92 | D 5000 | 1 | 3/1.8 |
| 64 | F | 4 | N | Y | 28/92 | 3000 | 1.5 | 1/0.8 | | | | |
| 65 | F | 6 | N | Y | 21/92 | 6000 | 0.6 | 1/0.6 | | | | |
| 66 | M | 8 | N | Y | 8/92 | 6000 | 1.5 | 1/0.8 | 16/92 | D | 0.8 | 2/0.6 |
| 67 | F | 5 | N | N | 12/92 | 0 | 2 | 1/0.5 | 17/92 | 0 | 1.5 | 0 |

# APPENDIX 3 Column key

| | |
|---|---|
| Pre RT US | Date of initial endoluminal ultrasound |
| Rx US 1 | Treatment at 1st ultrasound. Figure denotes laser energy in joules or D for dilatation |
| US1 T | Maximum tumour thickness at ultrasound 1 |
| US1 N | Maximum node thickness at ultrasound 1 |
| US 2 DATE | Date of 2nd endoluminal ultrasound |
| Rx US 2 | Treatment at 2nd ultrasound. Figure denotes laser energy in joules or D for dilatation |
| US2 T | Maximum tumour thickness at ultrasound 2 |
| US2 N | Maximum node thickness at ultrasound 2 |

# APPENDIX 4

## Quality of life data

| NO | RT | SUB | DG 1 | LASA 1 | QL 1 | DG2 | LASA 2 | QL 2 | DG CK | LASA CK | QL CK | DG 4 | LASA 4 | QL 4 | DG 5 | LASA 5 | QL 5 | DG 6 | LASA 6 | QL 6 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | N | C | | | | | | | | | | | | | | | | | | |
| 2 | N | B | | | | | | | | | | | | | | | | | | |
| 3 | N | C | | | | | | | 2 | | 8 | | | | | | | | | |
| 4 | N | A | | | | | | | 2 | 44 | 10 | 1 | | 8 | 1 | 34 | 6 | | | |
| 5 | N | B | 1 | 38 | 8 | | | | 2 | | 9 | | | | | | | | | |
| 6 | N | A | | | | | | | 1 | 46 | 9 | | | | | | | | | |
| 7 | N | B | | | | | | | | | | | | | | | | | | |
| 8 | N | A | 1 | 46 | 10 | | | | 0 | | 9 | | | | | | | | | |
| 9 | N | B | 1 | 34 | 7 | | | | | | | 2 | 36 | 7 | 2 | 46 | 6 | 1 | 38 | 8 |
| 10 | N | B | 0 | 42 | 9 | | | | | | | | | | | | | | | |
| 11 | N | C | 1 | 46 | 7 | | | | | | | | | | | | | | | |
| 12 | N | B | | | | | | | | | | 1 | 46 | 8 | | | | | | |
| 13 | N | A | 3 | 22 | 10 | | | | 2 | 46 | 9 | 4 | 43 | 8 | 3 | 40 | 7 | | | |
| 14 | N | B | 2 | 36 | 9 | | | | 2 | 36 | 8 | 2 | 36 | 8 | 3 | 20 | 7 | | | |
| 15 | N | C | | | | | | | | | | | | | | | | | | |
| 16 | N | A | | | | | | | 1 | 40 | 9 | 2 | 28 | 7 | 3 | 44 | 7 | | | |
| 17 | N | A | 1 | 38 | 9 | | | | 1 | 46 | 9 | 0 | 48 | 10 | 1 | 44 | 10 | 1 | 44 | 9 |
| 18 | N | B | 1 | 46 | 10 | | | | 1 | 40 | 9 | | | | | | | | | |
| 19 | N | A | | | | | | | 0 | 46 | 9 | 0 | 48 | 9 | 2 | 38 | 7 | | | |
| 20 | N | C | 2 | 38 | 9 | | | | 3 | 38 | 6 | 3 | | 2 | | | | | | |
| 21 | N | D | 2 | 32 | 5 | | | | 2 | 28 | 4 | | | | | | | | | |
| 22 | N | B | 2 | 40 | 8 | | | | 2 | 36 | 7 | 1 | 38 | 7 | 2 | 24 | 9 | 2 | 24 | 7 |
| 23 | N | B | 2 | 48 | 8 | | | | 2 | 42 | 8 | | | | | | | | | |
| 24 | N | A | 1 | 48 | 10 | | | | 0 | 44 | 10 | | | | | | | | | |
| 25 | N | B | | | | | | | 2 | 38 | 7 | 1 | | 9 | | | | | | |
| 26 | N | A | | | | | | | 1 | 46 | 10 | 2 | 40 | 10 | 2 | 40 | 9 | 3 | 30 | 8 |
| 27 | N | B | 1 | 42 | 6 | | | | 3 | 32 | 6 | 2 | 42 | 6 | 2 | 38 | 8 | | | |
| 28 | N | B | 2 | 44 | 10 | | | | 3 | 44 | 9 | 2 | 40 | 9 | | | | | | |
| 29 | N | B | | | | | | | | | | 2 | 33 | 9 | | | | | | |
| 30 | N | B | 1 | | 8 | | | | 1 | | 7 | 2 | | 6 | | | | | | |
| 31 | Y | B | 1 | 46 | 9 | 0 | 40 | 9 | | | | 2 | 34 | 9 | | | | | | |
| 32 | Y | A | | | | | | | | | | | | | | | | | | |
| 33 | Y | A | | | | 1 | 38 | 9 | 1 | 38 | 8 | | | | 2 | 24 | 6 | 2 | 40 | 7 |
| 34 | Y | A | 1 | 42 | 8 | 0 | 50 | 8 | 0 | | 10 | | | | | | | | | |
| 35 | Y | A | 1 | 40 | 9 | 1 | 44 | 6 | 0 | | 10 | | | | | | | | | |
| 36 | Y | C | | | | 1 | 22 | 3 | | | | 1 | | 8 | 2 | 32 | 4 | | | |
| 37 | Y | B | 0 | 44 | 9 | | | | 1 | | 8 | | | | | | | | | |
| 38 | Y | C | | | | | | | 1 | 26 | 8 | | | | | | | | | |
| 39 | Y | C | | | | 2 | 28 | 7 | | | | | | | | | | | | |
| 40 | Y | B | | | | 1 | 44 | 9 | 1 | 40 | 9 | 3 | 20 | 7 | | | | | | |
| 41 | Y | B | | | | | | | 0 | 32 | 9 | 2 | 46 | 10 | 1 | 40 | 10 | 2 | 42 | 9 |
| 42 | Y | B | 1 | 30 | 5 | 1 | 32 | 5 | 2 | 26 | 3 | 2 | 26 | 6 | | | | | | |
| 43 | Y | C | 2 | 40 | 6 | 2 | 38 | 6 | 3 | 14 | 1 | | | | | | | | | |
| 44 | Y | C | 3 | 42 | 9 | | | | | | | | | | | | | | | |
| 45 | Y | D | 1 | 48 | 8 | | | | | | | | | | | | | | | |
| 46 | Y | C | 2 | 38 | 6 | 2 | 38 | 6 | 0 | 42 | 6 | 2 | 28 | 3 | | | | | | |
| 47 | Y | A | 2 | 37 | 10 | 2 | 38 | 7 | 0 | 48 | 10 | 1 | 46 | 10 | 2 | 44 | 9 | 2 | 40 | 8 |
| 48 | Y | D | 2 | 40 | 8 | | | | | | | | | | | | | | | |
| 49 | Y | C | 2 | 43 | 9 | 2 | 40 | 8 | 2 | 34 | 9 | | | | | | | | | |
| 50 | Y | B | | | | 2 | 36 | 7 | 3 | 34 | 7 | 3 | 50 | 7 | | | | | | |
| 51 | Y | B | 1 | 40 | 6 | 1 | 28 | 6 | 3 | 40 | 6 | 2 | 44 | 5 | | | | | | |
| 52 | Y | A | | | | 0 | 46 | 10 | 0 | 46 | 10 | | | | 2 | 36 | 9 | 2 | 30 | 8 |
| 53 | Y | A | 1 | | 9 | 1 | 34 | 8 | 0 | 48 | 10 | 1 | 48 | 10 | 2 | 42 | 9 | | | |
| 54 | Y | C | 2 | | 9 | 3 | 36 | 8 | 2 | 32 | 7 | 3 | 34 | 8 | | | | | | |
| 55 | Y | B | | | | | | | 0 | 26 | 8 | | | | | | | | | |
| 56 | Y | C | 1 | 34 | 8 | 1 | 24 | 7 | 1 | 38 | 7 | 2 | 42 | 10 | 2 | 32 | 7 | 4 | 24 | 7 |
| 57 | Y | C | | | | | | | | | | | | | | | | | | |
| 58 | Y | A | | | | | | | 2 | 42 | 8 | | | | 2 | 40 | 9 | 2 | 42 | 9 |
| 59 | Y | C | 1 | 32 | 8 | | | | | | | | | | | | | | | |
| 60 | Y | B | | | | | | | 2 | 36 | 8 | 0 | 42 | 9 | | | | | | |
| 61 | Y | C | 2 | 15 | 7 | 1 | 21 | 7 | 1 | 28 | 8 | 2 | 12 | 3 | | | | | | |
| 62 | Y | C | | | | 2 | 32 | 6 | 2 | 48 | 5 | | | | | | | | | |
| 63 | Y | B | 1 | 34 | 8 | | | | 2 | 15 | 7 | 1 | 44 | 10 | 2 | 35 | 9 | | | |
| 64 | Y | B | | | | | | | 2 | 32 | 9 | | | | | | | | | |
| 65 | Y | B | | | | | | | | | | | | | | | | | | |
| 66 | Y | C | 3 | 31 | 5 | | | | | | | | | | | | | | | |
| 67 | Y | B | | | | 2 | 35 | 7 | 1 | 47 | 10 | 2 | | 8 | | | | | | |

# APPENDIX 5

## Cost data

| NO | AGE | SITE | HIST | METS | IP | RT | LT | CK | RXS PC | RX POST CK | COST CK | COST PC | FIBRES | COST IP | RT COST | CUFF | COST TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 75 | C | A | N | 35 | Y | 2 | D 2L | 4 | 3L T | 295 | 562 | 114 | 2905 | 830 | | 4706 |
| 2 | 65 | C | A | Y | 0 | N | 2 | 0 | 1 | L | 54 | 116 | 57 | 0 | 0 | | 227 |
| 3 | 66 | C | A | N | 42 | Y | 3 | D | 9 | 6L 2D T | 63 | 1036 | 114 | 3486 | 830 | | 5529 |
| 4 | 74 | C | A | N | 9 | N | 3 | 2L | 1 | L | 232 | 116 | 57 | 747 | 0 | | 1152 |
| 5 | 80 | C | A | N | 32 | Y | 3 | L | 0 | 0 | 116 | 0 | 57 | 2656 | 830 | | 3659 |
| 6 | 67 | ANA | A | N | 13 | Y | 3 | L | 2 | LT | 116 | 376 | 57 | 1079 | 830 | | 2548 |
| 7 | 75 | C | A | N | 20 | N | 5 | LD | 7 | 5L T TM | 330 | 848 | 114 | 1160 | 0 | 128 | 2670 |
| 8 | 84 | C | A | N | 53 | Y | 4 | 0 | 6 | 3L T TB TM | 54 | 670 | 57 | 4399 | 830 | | 6010 |
| 9 | 81 | C | A | N | 23 | N | 4 | 2L | 2 | 2L | 232 | 232 | 57 | 1909 | 0 | | 2430 |
| 10 | 66 | C | A | Y | 16 | Y | 4 | L | 0 | 0 | 116 | 0 | 57 | 1328 | 830 | | 2331 |
| 11 | 60 | C | A | N | 21 | N | 4 | D | 5 | 3D T TM | 63 | 457 | 0 | 1743 | 0 | | 2263 |
| 12 | 81 | C | A | N | 23 | N | 4 | 3L | 2 | T | 348 | 214 | 57 | 1909 | 0 | | 2528 |
| 13 | 85 | C | A | N | 22 | Y | 2 | L | 1 | T | 116 | 214 | 57 | 1826 | 830 | | 3043 |
| 14 | 67 | ANA | A | N | 5 | N | 3 | O | | | 0 | 0 | 0 | 415 | 0 | | 415 |
| 15 | 79 | C | A | N | 42 | Y | 7 | 0 | 4 | 2 DL 2L | 54 | 514 | 114 | 3486 | 830 | | 4990 |
| 16 | 58 | C | A | N | 33 | Y | 3 | DL | 1 | T | 141 | 214 | 0 | 2739 | 830 | | 3924 |
| 17 | 64 | C | A | Y | 37 | Y | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 3071 | 830 | | 3901 |
| 18 | 58 | ANA | A | N | 15 | N | 2 | 3L | 3 | 2L T | 348 | 446 | 114 | 1245 | 0 | | 2150 |
| 19 | 74 | C | A | N | 9 | Y | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 747 | 830 | | 1577 |
| 20 | 67 | ANA | A | N | 28 | N | 3 | 2L | 2 | 2L | 132 | 132 | 114 | 2324 | 0 | | 2702 |
| 21 | 82 | C | A | N | 7 | Y | 2 | 0 | 0 | 0 | 54 | 0 | 0 | 581 | 830 | | 1465 |
| 22 | 66 | C | A | N | 8 | N | 3 | - | 0 | 0 | 0 | 0 | 0 | 664 | 0 | | 664 |
| 23 | 72 | C | A | N | 24 | Y | 4 | 0 | 2 | LD L | 54 | 257 | 57 | 1992 | 830 | | 3190 |
| 24 | 70 | ANA | A | N | 25 | N | 3 | D | 6 | LD 2L D T | 63 | 640 | 57 | 2075 | 0 | | 2785 |
| 25 | 76 | LT | A | N | 34 | Y | 2 | D | 7 | 3D DL D L T | 63 | 723 | 57 | 2822 | 830 | | 4495 |
| 26 | 75 | C | A | Y | 9 | N | 4 | L | 1 | L | 116 | 116 | 57 | 747 | 0 | | 1036 |
| 27 | 69 | C | A | N | 8 | Y | 4 | - | 0 | 0 | 0 | 0 | 0 | 664 | 830 | | 1494 |
| 28 | 63 | C | A | Y | 18 | Y | 2 | - | 0 | - | 0 | 0 | 0 | 1494 | 830 | | 2324 |
| 29 | 78 | C | A | Y | 14 | N | 4 | 2L | 1 | T | 232 | 214 | 0 | 1162 | 0 | | 1608 |
| 30 | 60 | C | A | Y | 9 | N | 5 | 2 L T | | | 446 | 0 | 0 | 747 | 0 | | 1193 |
| 31 | 66 | C | A | Y | 13 | N | 2 | L | 4 | DL D L L | 116 | 436 | 114 | 1079 | 0 | | 1745 |
| 32 | 64 | C | A | N | 17 | N | 2 | 2L | 1 | L | 232 | 116 | 57 | 1411 | 0 | | 1816 |
| 33 | 74 | C | A | N | 4 | Y | 2 | L | 5 | 5L | 116 | 580 | 171 | 332 | 830 | | 2029 |
| 34 | 74 | C | A | N | 23 | N | 1 | 2L | 10 | 10 L | 132 | 1160 | 228 | 1909 | 0 | | 3429 |
| 35 | 65 | C | A | Y | 3 | Y | 2 | L | 0 | 0 | 116 | 0 | 57 | 249 | 830 | | 1252 |
| 36 | 73 | C | A | Y | 4 | N | 2 | DL L | 0 | 0 | 257 | 0 | 57 | 332 | 0 | | 646 |
| 37 | 50 | ANA | A | N | 21 | Y | 2 | L | 3 | 2D LD | 116 | 267 | 57 | 1743 | 830 | | 3013 |
| 38 | 66 | ANA | A | N | 4 | Y | 2 | - | 0 | | 0 | 0 | 0 | 332 | 830 | | 1162 |
| 39 | 73 | C | A | N | 14 | Y | 1 | 0 | 0 | | 54 | 0 | 0 | 1162 | 830 | | 2046 |
| 40 | 59 | ANA | A | N | 6 | Y | 2 | D | 0 | | 63 | 0 | 0 | 498 | 830 | | 1391 |
| 41 | 72 | LT | S | N | 29 | Y | 3 | D | 8 | 7L LT | 63 | 1072 | 171 | 2407 | 830 | | 4543 |
| 42 | 85 | C | S | N | 5 | N | 3 | D | | | 63 | 0 | 0 | 415 | 0 | | 478 |
| 43 | 83 | LT | S | N | 12 | N | 3 | LD | 2 | D T | 141 | 277 | 0 | 996 | 0 | | 1414 |
| 44 | 61 | LT | S | N | 23 | N | 6 | T | | | 214 | 0 | 0 | 1909 | 0 | | 2123 |
| 45 | 57 | C | S | Y | 7 | Y | 3 | L | 0 | 0 | 116 | 0 | 0 | 581 | 830 | | 697 |
| 46 | 88 | LT | S | N | 27 | N | 3 | LD L | 8 | 3L 3LD D T | 257 | 1050 | 171 | 2241 | 0 | | 3719 |
| 47 | 73 | LT | S | N | 23 | Y | 3 | D | 2 | L T | 63 | 330 | 57 | 1909 | 830 | | 3189 |
| 48 | 77 | C | S | N | 12 | Y | 2 | D | 1 | DL | 63 | 141 | 57 | 996 | 830 | | 2087 |
| 49 | 78 | LT | S | N | 24 | N | 5 | 2L | 3 | DL 2L | 232 | 373 | 114 | 1992 | 0 | | 2711 |
| 50 | 70 | C | S | N | 20 | Y | 7 | D | 2 | 2D | 63 | 126 | 0 | 1660 | 830 | | 2679 |
| 51 | 75 | C | S | N | 29 | Y | G | D | 3 | 3D | 63 | 189 | 0 | 2407 | 830 | | 3489 |
| 52 | 71 | LT | S | N | 11 | Y | 3 | D | 2 | 2D | 63 | 126 | 0 | 913 | 830 | | 1932 |
| 53 | 70 | LT | S | N | 34 | Y | 3 | 2 DL | 4 | 2D T TC TM | 282 | 608 | 57 | 2822 | 830 | | 4599 |
| 54 | 65 | LT | S | N | 9 | N | 2 | L | 0 | 0 | 116 | 0 | 57 | 747 | 0 | | 920 |
| 55 | 73 | LT | S | N | 6 | N | 4 | L | 3 | 2L T | 116 | 446 | 57 | 498 | 0 | | 1117 |
| 56 | 68 | LT | S | Y | 9 | Y | 2 | DL | 4 | 3D T | 141 | 403 | 57 | 747 | 830 | | 2178 |
| 57 | 55 | UT | S | Y | 13 | N | 2 | D L | 7 | 3L D T TM | 179 | 649 | 114 | 1079 | 0 | | 1793 |
| 58 | 69 | C | S | Y | 18 | N | 3 | DL | 4 | 2L LD D | 141 | 436 | 57 | 1494 | 0 | | 2128 |
| 59 | 77 | UT | S | N | 11 | N | 2 | DT | O | 0 | 214 | 0 | 0 | 913 | 0 | | 1127 |
| 60 | 78 | LT | S | N | 20 | Y | 2 | L | 1 | - | 116 | 0 | 0 | 1660 | 830 | | 2606 |
| 61 | 67 | LT | S | N | 21 | Y | 3 | 2D | 0 | 0 | 126 | 0 | 0 | 1743 | 830 | | 2699 |
| 62 | 82 | LT | S | N | 14 | Y | 2 | D | 0 | 0 | 63 | 0 | 0 | 1162 | 830 | 128 | 2183 |
| 63 | 67 | UT | S | N | 14 | N | 1 | DL | 4 | LD L D T | 141 | 584 | 57 | 1162 | 0 | | 1944 |
| 64 | 84 | C | S | N | 19 | Y | 2 | D | 2 | D T | 63 | 277 | 0 | 1577 | 830 | 128 | 2825 |
| 65 | 78 | LT | S | N | 13 | Y | 3 | D | 0 | 0 | 63 | 0 | 0 | 1079 | 830 | 128 | 2100 |
| 66 | 67 | UT | S | N | 13 | Y | 2 | D | 3 | D DL DT | 63 | 418 | 57 | 1079 | 830 | | 2447 |
| 67 | 78 | UT | S | N | 16 | N | 3 | L | 3 | 2D | 116 | 126 | 0 | 1328 | 0 | | 1570 |

# APPENDIX 5 Column key

See appendix 1 and 2 also........

ALL COSTS ARE IN POUNDS STERLING

| | |
|---|---|
| Cost CK | Cost of 'check endoscopy' procedures |
| Cost PC | Cost of all procedures after 'check endoscopy' |
| Fibres | Cost of laser fibres |
| Cost IP | Hospital stay costs |
| Cuff | Cost of cuffed tubes |
| Cost total | Total costs for the patient concerned |

# APPENDIX 6

## Rectal cancer study raw data

| PATIENTS NUMBER | ONE | TWO | THREE | FOUR | FIVE | SIX | SEVEN | EIGHT | NINE | TEN | ELEVEN | TWELVE | THIRTEEN |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NO | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
| AGE | 77 | 69 | 91 | 86 | 65 | 70 | 80 | 85 | 81 | 84 | 78 | 75 | 90 |
| SEX | M | F | F | F | M | F | M | F | M | M | M | M | F |
| LENGTH | 0-14 C3 | 14-17 C2 | 6-13 C3 | 11 C3 | 8 C3 | 6 C2 | 3 C3 | 4 C3 | 5 C3 | 6-10 C2 | 3-5 C2 | 7-9 Ana C3 | 5-9 C2 |
| HIST | VA | ANC | ANC | ANC | ANC | CX | ANC | ANC | ANC | ANC | ANC | ANC | ANC |
| SYMPTOMS | D | B | B urgency | D | B T | B | B | D Pain | B M | D T | B M | D | B |
| SYM DUR | Months | | 1 yr | 1 yr | 3/12 | 1/12 | 4 wks | ? | 4/12 | | | | |
| | | | | | | | | | | | | | |
| WHY LASER? | MED | FAILED LAP | INOP-LAP | AGE GEN | COAD/CLD | METS | ANA | AGE GEN | MED | MED | METS | ANA | METS |
| METS? | No | No | No | No | No | Yes | No | No | No | No | Liver/lung | No | Liver |
| DXRT DOSE:FRACTIONS | 30Gy:10f | 30Gy 10f | 30Gy:10f | 40Gy 6f | 55Gy in 20f | 30+30Gy | 50Gy 20f | 30Gy 10f | 30 Gy/10f | 30Gy/10f | 30Gy 10f | 30gy 10f | 30Gy 10f |
| RT TOL | G | G | G | G | G | G | G | G | G | G | G | G | G |
| DATE RT FINISHED | 43/90 | 39/90 | 48/90 | 50/91 | 10/91 | 41/90/50/9 | 51/90 | 52/90 | 14/91 | 38/91 | 34/91 | 6/92 | 40/91 |
| NO LASER PRE RT | 9 | 3 | 6 | 3 | 5 | 2 | 1 | 2 | 2 | 2 | 1 | 1 | 2 |
| TIME BEF RT | 39/52* | 17/52* | 15/52* | 14/52* | 14/52* | 13/52* | 0 | 2/52 | 6/52 | 14/52* | 3/7 | IMMED | IMMED |
| RX INT PRE RT | 4.3wks | 8/52 | 2.5wks | 3 wks | 3wks | 12 wks | | 2wks | 3 wks | 7wks | - | 0/52 | 6/52 |
| RX POST RT | 11 | 1 (+ 1 NO Rx ) | 5 | - | 5 | 2 | 4 | 1 | 4 | 3 | 0 - NO TUM | 1 | 0 |
| Energy / mo pre DXRT | 24,000 | 5,000 | 26,000 | 20,000 | 15,000 | 13,000 | NA | NA | NA | 2,500 | NA | NA | NA |
| Energy / mo post DXRT | 8,000 | 800 | 4,000 | 0 | 3,000 | 0 | 3,000 | 0 | 600 | 2,000 | 0 | 2,000 | 0 |
| TIME FU POST RT | 13/12 | 17/12 | 12/12 | 12/12 | 12/12 | 36/12 | 8/12 | 2.5/12 | 17/12 | 16/12 | 16/12 | 14/12 | 2/12 |
| RX INT POST RT | 5.5wks | 42 wks | 10wks | 53wks | 13w | 112wks | 9 wks | 9wks | 19wks | 14wks | 70wks | 7wks | 9 wks |
| SURVIVAL | 40/12+ | 20/12 | 15/12 | 14/12 | 15/12 | 28/12 | 10/12 | 2.5/12 | 18/12 | 20/12 | 17/12 | 14.5/12 | 3.5/12 |
| SYMPTOMS POST RT | Constip-st | OK | - | - | Constip | - | M-SLIGHT | pain | OK-Incont | OK | OK | freq | OK-fever |
| RT SUCCESS | NO | YES | YES | YES | YES | YES | YES | NO | YES | YES | YES | YES | PARTIAL |
| RT Comps | Stricture | - | Stricture | - | Stricture | - | - | - | - | - | - | Stricture Colostomy | - |
| | | Also had Chemo | | | | | | | | | | | |

# APPENDIX 6 Column key

| | |
|---|---|
| Hist | Histology: VA=Villous adenoma ANC= Rectal adenocarcinoma CX =Cervical adenocarcinoma |
| Symptoms | M=Mucous B=Bleeding T=Tenesmus D=Diarrhoea |
| Time bef RT | Duration of treatment with laser only prior to radiotherapy. Seven starred patients received laser for 3 months or more prior to radiotherapy |
| Rx int pre RT | Time between laser treatments prior to radiotherapy |
| RX post RT | Number of endoscopic treatments after radiotherapy |
| Energy/mo | Mean laser energy in joules applied per month before and after radiotherapy |
| Rx int po RT | Time between endoscopic treatments after radiotherapy |

# APPENDIX 7

Tube overgrowth raw data

| no | age | sex | site | LENGTH | hist | WHY PALLIATION | TOP OF TUBE | T ins rec dys | OTHER | DG1 | DG2 | DG3 | LT NO | SURVIV |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 70 | M | A | 5 | A | AGE MED | 26 | 4/12 | | 4 | 2 | 2 | 2 | 3/52 |
| 2 | 75 | M | C | 5 | A | AGE MED | | | | 4 | 2 | 2 | 5 | 9/52 |
| 3 | 60 | M | LT | ? | S | AGE MED | 32 | 4/12 | | 4 | 2 | 2 | 2 | 3/52 |
| 4 | 79 | F | C | ? | A | AGE MED | 27 | 4/12 | OVERGROWN AT BOTTOM | 4 | 2 | 2 | 1 | 3/52 |
| 5 | 75 | M | ANA | 2 | A | ANA | 28 | 4/12 | | 4 | 3 | 3 | 1 | 3/52 |
| 6 | 83 | M | C | 2 | S | AGE MED | 29 PULLED UP TO 25 | 14/12 | FIRST TUBE 35/12 BEFORE REF | 4 | 2 | 1 | 1 | 34/52 |
| 7 | 79 | M | C | 3 | A | AGE MED | 31 PULLED UP TO 26 | 8/12 | | 3 | 1 | 2 | 2 | 36/52 |
| 8 | 79 | F | C | 4 | A | AGE MED | 32 | 7/12 | | 4 | 2 | 2 | 3 | 20/52 |
| 9 | 90 | M | C | 3 | A | METS | 32 | 7/12 | | 3 | 2 | 2 | 4 | 14/52 |
| 10 | 78 | F | C | 4 | A | EXT(LAP) | 30 | 4/12 | OVERGROWN BOTH ENDS MAINLY TOP | 2 | 2 | 2 | 5 | 24/52 |
| 11 | 46 | M | C | ? | A | EXT(LAP) | 35 | 3/12 | OVERGROWN BOTH ENDS MAINLY TOP | 4 | 3 | 3 | 2 | 10/52 |
| 12 | 62 | M | ANA | 5 | A | ANA | 36 | | | 4 | 3 | 3 | 2 | 6/52 |
| 13 | 75 | M | LT | 3 | S | METS | 20 PUSHED DOWN | 7/12 | OVERGROWN BOTTOM | 3 | 2 | 2 | 1 | 5/52 |
| 14 | 75 | M | C | 3 | A | AGE MED | 30 | 9/12 | | 1 | 2 | 3 | 1 | 8/52 |

# APPENDIX 7 Column key

Keys as for appendix 1 , 2 and 3 and in addition -

| | |
|---|---|
| T ins rec dys | Duration in months between tube insertion and recurrent dysphagia |
| DG1 | Initial dysphagia grade |
| DG 2 | Dysphagia grade after laser treatment |
| DG 3 | Mean dysphagia grade during remaining survival |

# APPENDIX 8

**Publications arising from the studies described in this thesis.**

1) Radiation enhancement of laser palliation for malignant dysphagia: A pilot study. IR Sargeant, LA Loizou, J Tobias, G Blackman, S Thorpe and SG Bown. Gut 1992;33:1597-1601.

2) Combined laser and radiotherapy for palliation of malignant dysphagia : a randomised study. IR Sargeant, J Tobias, G Blackman, S Thorpe and SG Bown. Gut 1992 33 ;1:S51 (abst) ; British Journal of Cancer 1992 66;17:46 (abst) and paper in preparation.

3) Non-optic endosonography in advanced carcinoma of the oesophagus. JR Glover, IR Sargeant, SG Bown and WR Lees. GI Endoscopy 1994;40:194-198.

4) An economic evaluation of Nd YAG laser ablation versus endoscopic intubation for the palliation of malignant dysphagia. Submitted to Gut May 1994. Sculpher MJ, Spencer GM, Sargeant IR, Loizou LA, Thorpe SM and Bown SG.

5) Radiation enhancement of laser palliation for advanced rectal and rectosigmoid cancer:a pilot study. IR Sargeant, LA Loizou, J Tobias, G Blackman, S Thorpe and SG Bown. Gut 1993;34:958-962.

6) Combination Laser and Radiotherapy for Palliation of Advanced Rectosigmoid and Oesophageal cancers. IR Sargeant, JS Tobias and SG Bown. Current Radiation Oncology Vol 1, Edward Arnold publications 1994 Ch 12 p 182-202. Editors Tobias and Thomas.

7) Cuffed oesophageal prosthesis: a useful device in desperate situations in oesophageal malignancy. IR Sargeant, SG Bown, S Thorpe. Gastrointestinal Endoscopy 1992;38:669-75.

8) Recanalisation of tube overgrowth: a useful new indication for laser in palliation of malignant dysphagia. IR Sargeant, LA Loizou, M Tulloch, S Thorpe and SG Bown.Gastrointestinal Endoscopy 1992;38:165-170.

# APPENDIX 9

## Statement describing the Author's individual contribution to the studies in this thesis

None of the studies in this Thesis, either in whole or in part have previously been submitted for a degree. As with most clinical research, the studies in this Thesis were the result of cooperation between a number of individuals.

Overall more than 2/3 of the endoscopic procedures were personally performed by the author.

The patients with oesophagogastric cancer were either treated, or their treatment closely supervised, by one of 3 endoscopists, Dr LA Loizou, Professor SG Bown and the author. The treatment of all patients enroled into studies since November 1989 was performed or closely supervised by the author or Professor Bown.

Endoluminal ultrasound examinations were performed with the assistence of a radiologist (Dr B Lees or Dr J Glover). The probe was passed by the author on 90% of occasions.

All the studies except the pilot study of laser and radiotherapy for oesophageal cancer were conceived, organised and conducted by the author and Professor Bown. The pilot study referred to was set up by Dr LA Loizou who entered most of the patients. Many follow up procedures were performed by the author as was data collection and analysis.

While the economic evaluation of laser versus laser and external beam radiotherapy was performed by the author many of the costings for procedures had already been calculated by Dr M Sculpher of the health economics research group at Brunel University.

*Reprinted from Gut, December 1992, Vol. 33, No. 12, Pages 1597-1601*

# Radiation enhancement of laser palliation for malignant dysphagia: a pilot study

I R Sargeant, L A Loizou, J S Tobias, G Blackman, S Thorpe, S G Bown

**Abstract**

**Laser therapy offers rapid relief of dysphagia for patients with cancers of the oesophagus and gastric cardia but repeat treatments are required approximately every five weeks to maintain good swallowing. To try to prolong the treatment interval, 22 elderly patients were given additional external beam radiotherapy. Nine had squamous cell carcinoma and 13 adenocarcinoma: five had documented metastases. Six received 40 Gy and 16,30 Gy in 10–20 fractions. A 'check' endoscopy was performed three weeks after external beam radiotherapy. Dysphagia was graded from 0–4 (0=normal; 4=dysphagia for liquids). The median dysphagia grade improved from 3 to 1 after laser treatment. This improvement was maintained in the 30 Gy group but there was a noticeable deterioration in three of those who had received the higher radiation dose. A lifelong dysphagia grade of 2 or better was enjoyed by 14 of 16 patients in the 30 Gy group but only two of six in the 40 Gy group. The dysphagia controlled interval was 9 weeks (median) after check endoscopy and subsequent endoscopic procedures were required every 13 weeks to maintain good swallowing. There were no endoscopy related complications. Combined treatment is a promising approach for reducing the frequency of endoscopic treatments. The 30 Gy dose seems more appropriate and may prolong survival. A randomised study to test these conclusions is in progress.**

(*Gut* 1992; 33: 1597–1601)

Carcinomas of the oesophagus and gastric cardia become symptomatic late in their natural history and commonly occur in the elderly who are unfit for surgery. Consequently, around 60% of these patients are deemed unsuitable for a curative attempt with surgery or radical radiotherapy at presentation.[1] There are now many treatments available for palliation of this difficult condition. Laser treatment offers rapid and effective relief of dysphagia, it can be performed as an outpatient procedure, it does not have systemic effects, and serious complications occur in only about 1% of procedures. However, one major drawback of laser is the need for repeat treatments every five weeks or so in most patients to maintain good swallowing.[2-4] Although laser is effective at tumour debulking, disease remains in the oesophageal wall and beyond the lumen in local nodes and thus tumour regrowth occurs fairly rapidly. Radiotherapy, however, has the potential for treating all the oesophageal tumour and the local regional draining sites[5] and, thus, should be complimentary to laser. Further clinical data to support this argument have been outlined in a recent review.[6]

External beam radiotherapy alone relieves dysphagia slowly, often taking several weeks for maximal effect.[7] A recent study of palliative radiotherapy[8] suggested that patients with relatively good swallowing enjoy improved survival over those who swallow poorly at presentation. There is, thus, both theoretical and clinical evidence to support the view that a patient whose swallowing has been improved by laser recanalisation should benefit further from radiotherapy. There has, however, been only one report[9] to date in which the combination of laser and radiotherapy has been studied and intraluminal rather than external beam radiotherapy was used. Intraluminal radiotherapy (brachytherapy) causes superficial damage to the tumour as there is a rapid fall off in dose with distance from the source and it is not as effective in terms of irradiating the whole tumour as external beam treatment. The authors did, however, report benefit in terms of a prolonged 'dysphagia free interval' with additional brachytherapy in patients with squamous cell oesophageal cancers recanalised with laser. The present study was initiated to determine if palliative external beam radiotherapy, a more widely available and practical technique, reduces the need for frequent follow up procedures after laser treatment alone. All patients with a technically satisfactory result and who could swallow fluids or better after laser treatment were considered for additional radiotherapy.

## Methods

### PATIENT SELECTION

The laser unit at University College Hospital acts as a tertiary referral centre for patients suffering from malignant dysphagia who are considered unsuitable for surgery. A smaller number of patients treated with laser (around 20%) present directly to the hospital. Patients recruited into this study were initially seen by us between September 1988 and June 1989. Patients with predominantly exophytic carcinomas of the oesophagus and gastric cardia thought suitable for laser treatment were eligible for the study. All patients recruited were deemed inoperable either because of advanced disease or because they presented an unacceptable anaesthetic risk. Five patients had documented metastatic disease, five had advanced local disease detected at computed tomography, and three had undergone laparotomy and their tumours could not be resected. A further nine were considered unsuitable for surgery because of age or general debility, or both. Patients with a good technical result from

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TABLE I *Demographic patient data*

| | |
|---|---|
| Total no | 22 |
| Male/female | 15/7 |
| Mean (SD) age (years) | 68 (11) |
| Squamous call carcinoma/adenocarcinoma | 9/13 |
| Cardia/thoracic | 15/6 (1 anastomotic) |
| Mean (SD) tumour length (cm) | 7 (3) |
| Metastases | 5 |
| Inoperable – CT or at Laparotomy | 8 |
| Medically unfit | 9 |

*CT=computed tomogram.*

laser treatment who swallow fluids, or better, were assessed for radiotherapy by a consultant radiotherapist (JST) before trial entry. Those who had had previous radiotherapy were excluded. All patients had either squamous cell carcinoma of the oesophagus or adenocarcinoma of the cardia. Patients with malignancy arising in organs other than the oesophagus and that caused dysphagia by direct invasion or metastatic spread were excluded. Full demographic data are given in Table I.

*Ethical aspects*

All patients were told about the nature of the study. Formal ethical committee approval was not considered necessary as both treatments are well established therapies for oesophageal cancer and all patients entered into the study were treated identically (no randomisation).

ENDOSCOPIC TECHNIQUE

The laser technique has been published in detail elsewhere.[13] Treatment was performed under sedation with diazemuls/pethidine using an Olympus 1T 20 endoscope (KeyMed Ltd, Southend, UK). A flexilase Nd: YAG laser (Living Technology, Glasgow) was used in conjunction with a delivery system comprising a 0·4 mm quartz fibre contained in a 2·2 mm Teflon catheter. The distal end of the fibre, which protrudes beyond the tip of the endoscope during treatment, is protected by a metal tip that allows a coaxial stream of gas to be passed around the fibre to cool the tip and clear the target of blood and debris. Venting of gas was achieved by means of a tube attached via a three way tap to the working channel of the endoscope. The gas was vented through an underwater drain to remove debris and then out of the endoscopy room through a specially designed extractor fan. It is usual practice to begin laser treatment at the distal end of the tumour and proceed proximally as laser induced swelling may prevent passage of the scope. In cases where the tumour could not be negotiated with the endoscope, a guide wire was passed and the oesophagus was dilated to 18 mm with Celestin dilators. Polypoid areas were vaporised shaving them back to within 2–3 mm of the oesophageal wall. Raised flat areas of tumour were coagulated and left to slough off (within a few days of treatment). Patients underwent laser sessions as appropriate to destroy intraluminal tumour and restore oesophageal patency before consideration for radiotherapy.

RADIOTHERAPY

All patients were irradiated using supervoltage teletherapy (cobalt 60). The target volume was determined by the length of tumour with a 5 cm margin at the upper and lower border of the tumour and a 3 cm margin circumferentially. The treatment was delivered by anterior and posterior opposed fields in all cases. In the early part of the study patients were initially given 20 Gy in five or 10 fractions and six patients who had tolerated this dose well were given a further 20 Gy dose either immediately or four to six weeks later (total dose 40 Gy). It soon became apparent that most of these patients could not tolerate this total dose and subsequent patients all received 30 Gy in 10 fractions. Twenty patients had to stay in hospital for treatment. This increased the median lifetime total hospital stay to 21 days in comparison with historical inpatient times of around 14 days for laser only.

FOLLOW UP

All patients underwent follow up endoscopy three weeks after completing of radiotherapy (check endoscopy). Endoscopic findings were recorded as at the initial endoscopy, and further laser treatment was applied only to polypoid tumour. All patients were subsequently contacted monthly by the research sister (ST) to assess progress and the necessity for further treatment. The dysphagia score was recorded according to the scale previously used by us (0=normal; 1=most solids; 2=semi-solids; 3=liquids only; 4=difficulty with liquids). Patients whose dysphagia grade deteriorated by one or more points or who felt that their swallowing had deteriorated significantly were re-endoscoped for assessment and further therapy as appropriate.

## Results

DYSPHAGIA GRADES

The median dysphagia grade for all patients before laser treatment was 3 (liquids only) and this improved to a median of 1 (most solids) after laser treatment. The spectrum of dysphagia at presentation was very similar in patients treated with radiotherapy at the 30 Gy and 40 Gy dosage levels. After radiotherapy there was very little change in the dysphagia grades in the group treated with 30 Gy but three of the six receiving 40 Gy showed a noticeable deterioration and could swallow only fluids until their death. If a mean dysphagia grade of 2 (semi-solid diet) for the duration of each patient's survival is regarded as a success, 14 of 16 in the 30 Gy group and two of six in the 40 Gy group enjoyed a successful outcome. This difference is significant at the 5% level ($\chi^2$ test).

TABLE II *Dysphagia controlled interval (DCI) (weeks) after 'check' endoscopy for all patients and broken down according to history*

| | Squamous cell carcinomas | Adenocarcinomas | All patients |
|---|---|---|---|
| All patients (median (range)) | 17 (1–170) | 9 (2–26) | 9 (1–170) |
| 30 Gy dose group only | 20 (3–170) | 11 (2-23) | 13 (2–170) |
| Historical 'laser only' controls | 5 | 5 | 5 |

TABLE III *Survival data according to subgroup*

| | *Laser +30 Gy* | *Laser +40 Gy* | *Laser only* |
|---|---|---|---|
| Patient no | 16 | 6 | 43 |
| Median (range) survival (weeks) | 44 (8–170*) | 19 (7–73) | 22 (4–117) |
| 1 year survivors | 5/16 (30%) | 1/6 (16%) | 5/43 (12%) |

** One patient still alive at 170 weeks (see text).*

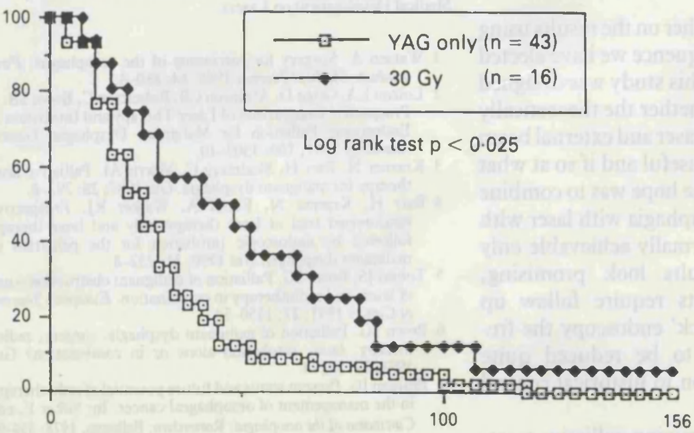
Three patients entered into this study were swallowing only fluids after initial laser recanalisation. One received the higher radiotherapy dose. Although radiotherapy was tolerated well by two of them, swallowing did not improve with treatment. One was eventually intubated and the other two enjoyed only short survival (eight and nine weeks respectively).

DYSPHAGIA CONTROLLED INTERVAL AND NECESSITY FOR REPEAT ENDOSCOPY

The dysphagia controlled interval for the purpose of this study was the time between the 'check' endoscopy and the next follow up endoscopy, performed when the patient complained of further deterioration of swallowing, or to death if the patient never required another endoscopy. The figures for all patients broken down according to histology and radiotherapy dosage are shown in Table II and data from historical laser only patients[2] are also given. Overall, patients treated with radiotherapy have a dysphagia controlled interval of 9 weeks (median) and for patients receiving the 30 Gy dose this is slightly longer (11 weeks). The dysphagia controlled interval was even longer (median 17 weeks) in patients with squamous cell carcinomas, although numbers are small.

Eleven patients required no further treatment after check endoscopy (one is still alive) and the median survival in this group was 9 weeks. Considering all those who required further endoscopic treatment after the check endoscopy, the median interval between follow up procedures required was 13 weeks (range 4–67). Eight patients required dilatation at check endoscopy but only three of these had fibrous strictures only, the rest having regrowth of tumour as well. Overall, 13 patients required further endoscopic treatment for tumour after radiotherapy. Three patients who developed severe dysphagia from extrinsic strictures were intubated (at 5 weeks, 5 months, and 14 months after start of treatment). All swallowed well with tubes (dysphagia grade 2). Two survived several more months but the third died a few weeks after intubation. All but one of the patients have died at the time of writing. None died of aspiration, all gradually weakened with cancer cachexia or the effects of metastatic disease, or both.

*Figure 1: Survival curves, laser (YAG) +30 Gy radiotherapy and historical laser only controls.*




SURVIVAL

This study was not set up to assess survival but it became apparent that patients in the 30 Gy group were doing well and it was decided to examine survival data in detail. Table III shows the crude survival data from presentation for each group receiving radiotherapy and for historical laser only controls, again taken from our earlier study.[2] These data give the impression of improved survival in the 30 Gy group and therefore survival curves were plotted (Figs 1 and 2). These curves were analysed using the log rank test and this shows a significantly ($p<0{\cdot}025$) prolonged survival in the group receiving the 30 Gy dose compared with historical controls. As the study was not randomised it could reasonably be argued that this difference is at least partly due to differences in selection. There was no statistical difference between the groups receiving different doses of radiotherapy, although the survival of patients receiving 40 Gy is generally shorter. One patient in the 30 Gy group is still alive. She is a 78 year old who presented with a 3 cm squamous cell cancer and has remained well for 170 weeks with entirely normal swallowing since treatment at three laser sessions followed by the radiotherapy.

COMPLICATIONS

No perforations were experienced in this group of patients. Mild nausea, lethargy, and odonyphagia were common during radiotherapy but usually did not amount to more than a minor irritation for most patients. Radiotherapy was poorly tolerated in three of the six patients who received the higher radiotherapy dose. They never really recovered after radiation, most did not swallow well and succumbed fairly rapidly from cachexia. Only two of the 16 who received the 30 Gy dose had more than minor symptoms. One of these succumbed early with poor swallowing but the other recovered and eventually died swallowing well 24 weeks after treatment.

Fibrous strictures were identified in three patients at the 'check' endoscopy and another five had fibrous narrowing as well as further luminal tumour growth. Two of those with fibrous strictures required no further treatment after dilatation at the 'check' procedure and the third needed dilations every 9 weeks for a year.

## Discussion

There are many techniques available for the palliation of patients with cancer of the oesophagus and gastric cardia. In addition to the Nd YAG laser, these include intubation with prosthetic tubes, external beam radiotherapy, and

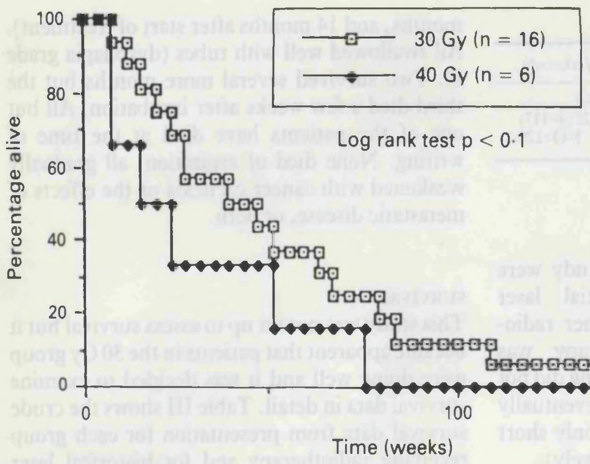



*Figure 2: Survival curves, laser (YAG) +30 Gy radiotherapy and laser +40 Gy radiotherapy.*

intracavitary radiotherapy (brachytherapy). The important parameters to consider in assessing these techniques are the quality of swallowing achieved, which is well reflected in the overall quality of life[2 4] and the price paid to achieve that quality (number of endoscopies, time in hospital for procedures, procedure related complications). Intubation, while offering rapid relief, does not allow many patients to take solids.[2] In addition, there is a higher risk of procedure related perforation than with laser (13% *v* 2% for laser in a series at this unit[2]). Potentially serious long term complications of tube are reported in all series and comprise tube displacement (3–19%), overgrowth (2–7%), and late perforation (0–7%).[2 4 11–13] Brachytherapy[9 14] looks promising but can cause severe oesophagitis and little data are yet available on the quality of palliation.

It is only recently that researchers have started to compare techniques in similar patient groups. A study from our unit comparing laser with intubation[2] has given us a better idea of which patients are likely to benefit most in terms of quality of swallowing from each of these methods. Those patients who do well with laser achieve a quality of swallowing that is better than the best attainable by tube. The quality of swallowing achieved with a tube is much more consistent (semi-solid diet) but only a few patients can swallow any solids. The availability of two treatments can thus be used to maximise palliation in individual patients. In our unit it is now standard policy to intubate patients who fail to manage at least a semi-solid diet with laser therapy.

In order to improve further on the results using different techniques in sequence we have elected to combine treatments. This study was designed to give an indication of whether the theoretically attractive combination of laser and external beam radiotherapy is clinically useful and if so at what dose. More specifically, the hope was to combine the better palliation of dysphagia with laser with more prolonged relief normally achievable only with a tube. The results look promising, although 50% of patients require follow up procedures after the 'check' endoscopy the frequency of these seems to be reduced quite dramatically in comparison to historical control data.

As these patients are receiving palliative treatment, it is important not to be so aggressive that the side effects of radiotherapy detract significantly from the benefit achieved with laser, either in terms of deterioration in general condition or dysphagia. The results indicate that the 30 Gy dose in 10 fractions is well tolerated in this patient group. Our limited experience of higher doses in this palliative setting is not favourable, although the numbers treated were small. Overall, the dysphagia controlled interval is prolonged and the subsequent necessity for follow up endoscopy is reduced, particularly for squamous cell cancers in comparison to historical control data. It is of interest that the brachytherapy study mentioned[9] showed a prolonged 'dysphagia free' interval but only for patients with squamous cell tumours. One concern of applying two treatments which can induce fibrosis was that we would have an unacceptable number of fibrous strictures but that was not the case. Only three patients came back with sole 'fibrous' narrowing at the check endoscopy. Overall, 13 patients required further laser for tumour after external beam radiotherapy. This suggests that the radiotherapy may be slowing tumour regrowth rather than causing wholesale tumour necrosis.

The survival curves for the 30 Gy group and 43 historical controls indicate the possibility of increased survival with external beam radiotherapy. However, it is important to treat comparisons with historical data with caution in view of possible differences in patient selection.

The results of this pilot study are promising and indicate that a randomised study to evaluate the combination of laser and external beam radiotherapy at the 30 Gy dose in 10 fractions in a larger number of patients would be worthwhile. Such a study is already underway. In view of others' experience[8] and our own with patients with dysphagia grade 3 who received radiotherapy, we have elected to randomise only patients who are able to swallow a semi-solid diet, or better, after laser.

Other endoscopic techniques for relieving swallowing such as alcohol injection or BICAP probe have been shown effective in the palliation of malignant dysphagia.[14 15] It is likely that any benefit seen with radiotherapy in combination with laser would be mirrored for such techniques and appropriate studies with these combinations should be encouraged.

All authors were supported by the Department of Health Special Medical Development on Lasers.

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0016-5107/92/3802-0165$03.00
GASTROINTESTINAL ENDOSCOPY


# Recanalization of tube overgrowth: a useful new indication for laser in palliation of malignant dysphagia

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**Overgrowth of an esophageal prosthesis by cancer is a late complication of insertion which presents a difficult management problem. We have treated 14 such patients; 9 had Celestin tubes and 5 Atkinson tubes in situ for a median of 7 months. The median patient age was 75 years; 3 had squamous cell carcinomas and 11 adenocarcinomas; 12 were at the lowest thoracic esophagus or cardia, and 2 were anastomotic. Eleven tubes were overgrown at the top, two at the bottom only, and one at both ends. Dysphagia was graded from 0 to 4 (0 = normal; 4 = dysphagia for liquids). All patients but one improved with treatment. The median pre-treatment grade was 4 (range, 2 to 4) and post-treatment was 2 (0 to 3). This improvement was significant ($p < 0.01$ Wilcoxon-signed rank). Most patients required only one or two endoscopies. The median survival was 9 weeks from first laser session (range, 3 to 36 weeks). We feel these results justify laser treatment in most patients in whom cancer overgrowth causes blockage of an esophageal prosthesis. (Gastrointest Endosc 1992;38:165–169)**

Esophageal prostheses are an effective and often lifelong method of relieving dysphagia in patients with cancers of the esophagus and gastric cardia. The quality of swallowing is not always as good as after laser therapy, but we would advocate routine use of tubes in patients who have not responded well to laser.[1] Many units do not have access to laser facilities and most patients in the United Kingdom are palliated by intubation as first line treatment. Overall 15 to 50% of patients[1-4] suffer tube complications or malfunction. Perforation at intubation occurs in up to 11% of patients and late perforation in up to 7%. Tube blockage and migration are the most common late complications. Food bolus obstruction can usually be cleared with ingestion of carbonated fluids or of a small quantity of hydrogen peroxide diluted in water. If this fails the tube can be cleared endoscopically. Migration occurs less frequently (3 to 19%) and requires tube repositioning or replacement, although some of these patients may be better managed with laser treatment. Tube overgrowth occurs in a small but significant number of patients and is often difficult to deal with. The incidence of tube overgrowth varies between series but most authors document such cases. Ogilvie et al.[2] recorded 7 cases in 118 patients (6%) but Gasparri et al.[4] described only 5 cases in 248 intubated patients (2%). In our own study of laser versus tube,[1] overgrowth was seen in 2 of 30 (7%) of those intubated. Patients usually present with this problem many months after intubation, and the value of further therapeutic measures has not been determined. We undertook this prospective study to assess the value of laser therapy in this group.

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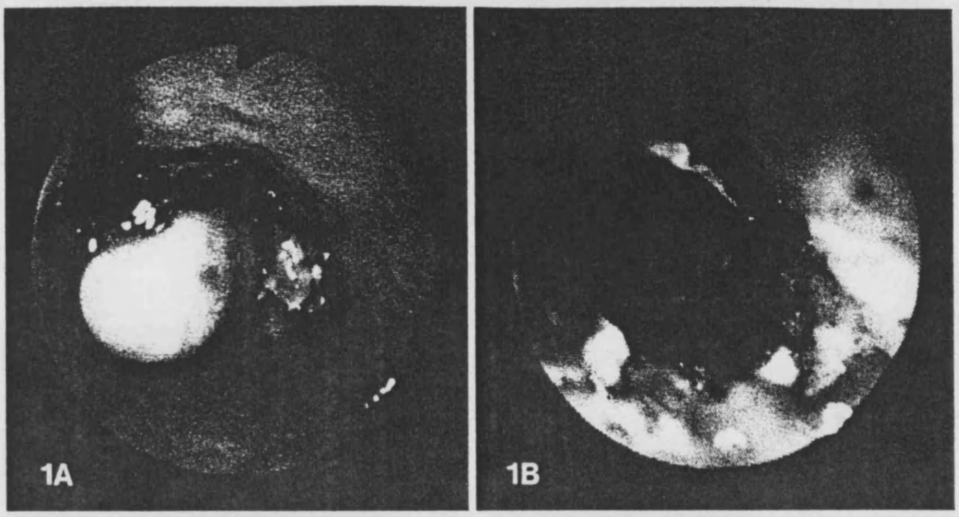
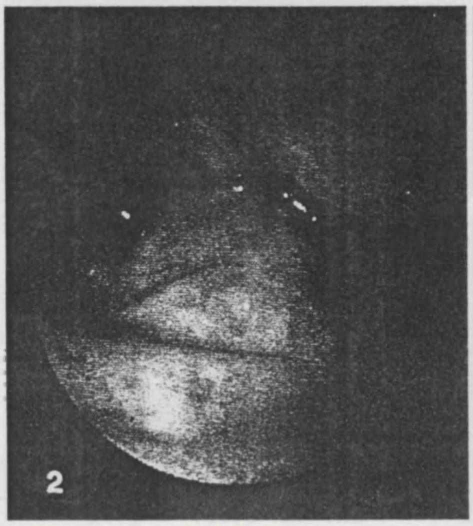
## PATIENTS

We studied 14 patients with tube overgrowth seen in this unit between December 1986 and April 1991. Twelve patients had been intubated at other centers and two had overgrowth following intubation by us. Tube position had been documented endoscopically in all patients after insertion. All patients were re-endoscoped when they developed overgrowth, and assessment of the tubes at that time con-



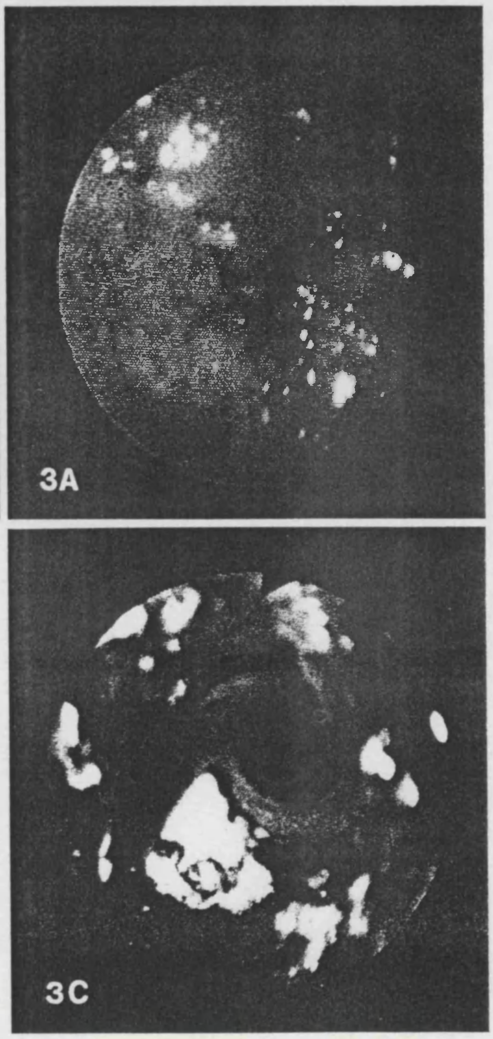




**Figure 1.** *A*, This is a typical polypoid tumor overgrowing a Celestin tube in an 83-year-old man who presented with recurrent dysphagia 14 months after tube insertion for an adenocarcinoma of the cardia. *B*, This demonstrates the result following laser of the tumor shown in *A*. This tube was one of those shifted up (in this case by 5 cm) to entirely cover the overgrown area. A further overgrowth occurred and the patient required repeat laser treatment 20 weeks later but he survived a total of 36 weeks after the first laser treatment. He was swallowing a semi-solid diet for almost all that time.

**Figure 2.** Some overgrowths are not so easily recognized. This shows what may have been dismissed as a fold of normal mucosa or edematous swelling resulting from pressure necrosis. This appearance occurred above an Atkinson tube which had functioned well for 7 months for a 79-year-old woman with an adenocarcinoma at the cardia. The lesion could not be passed

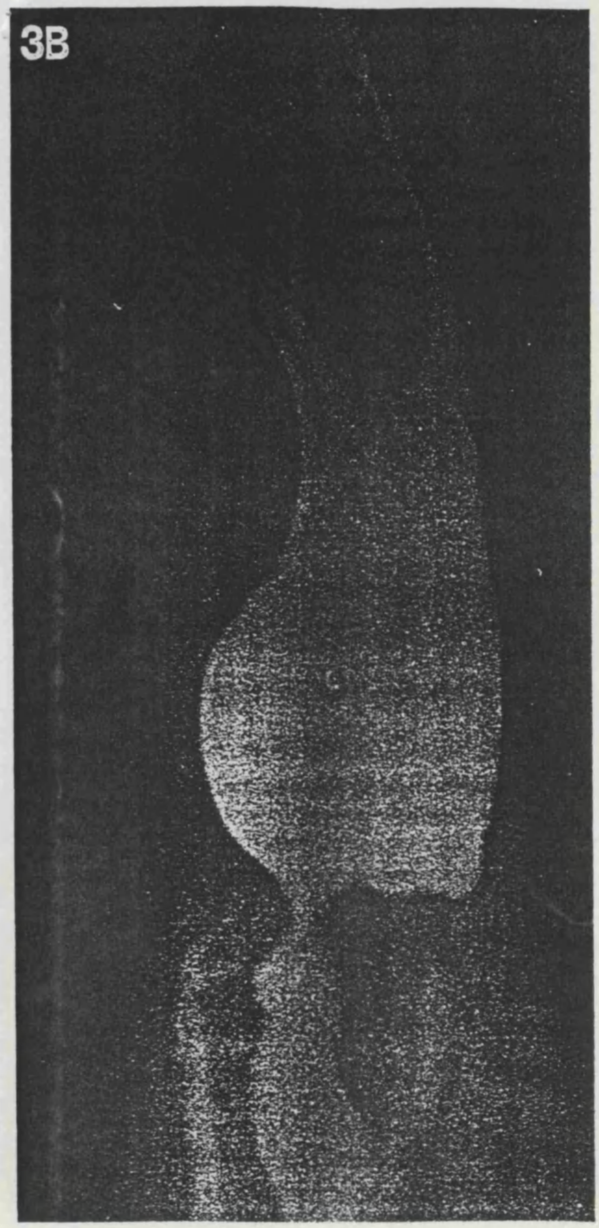


Figure 3B.

firmed none of them had displaced. All patients with displaced tubes were excluded.

The median patient age was 75 years (range, 46 to 90 years); 11 were men and 3 were women. Eleven patients had adenocarcinomas and three had squamous cell carcinomas. Twelve tumors were in the lower thoracic esophagus or cardia and two patients had anastomotic recurrences following previous surgery. It is unusual for such patients to undergo a second resection in the United Kingdom. Ten patients were deemed unsuitable for surgery due to age and general condition and had been intubated endoscopically, two had been found to have inoperable tumor at laparotomy and a tube had been inserted during the operation (and sutured in place). Nine tubes were Celestin and five were Atkinson in design. All patients were well palliated immediately following tube insertion; none were unable to manage a semi-solid diet.

The median time from intubation to referral with an overgrown tube was 7 months (range, 4 to 14 months). Eleven tubes were overgrown at the top, two at the bottom, and one at both ends. The median length of the tumor beyond the end of the tube was 3 cm (range, 2 to 5 cm).

## TECHNIQUES

The laser technique has been published in detail elsewhere.[5] Overgrown areas are often polypoid and it is safe to vaporize nodules, shaving them back to within 2 to 3 mm of the esophageal wall. Raised flat areas of tumor can be coagulated and will slough within a few days of treatment. It is usual practice to commence laser treatment at the distal end of the tumor and proceed proximally as laser-induced swelling may prevent passage of the endoscope. Overgrown tubes cannot usually be negotiated with the endoscope, and thus treatment normally has to be started at the proximal end. This does not usually cause a problem as overgrown segments are short and following vaporization of nodules the scope will often pass through the stricture at the end of one session. Tubes overgrown at the bottom require a smaller caliber endoscope as the Olympus 1T 20 endoscope (KeyMed Ltd., Southend, U.K.) normally used for laser treatment will not pass through either Atkinson or Celestin tubes. Angulation of the endoscope while confined within the tube is limited, and targeting can be more difficult than similar growths above the tube. In order to achieve the best lumen, some patients also underwent tube manipulation and one had a second tube inserted above the first; the details of this are given below. All tube manipulation was performed with an Atkinson introducer. This presented no problem for Atkinson tubes but as Celestin tubes have a slightly larger internal diameter it was necessary to wrap some micropore tape around the olive at the distal end of the inserter to allow enhanced grip on the tube. Even with this technique,

with the endoscope and had a hard consistency. It was treated, tentatively at first, with laser. As treatment progressed the fold was seen to be obviously neoplastic and a considerable amount of laser energy was applied (18,000 joules) to vaporize the whole area. We would stress that extreme care must be taken when treating such lesions. If there is doubt about the nature of such a lesion, it may be safer to resort to tube manipulation or replacement instead.

**Figure 3.** *A*, This shows the appearance of tumor overgrowing an Atkinson tube which had provided good palliation for 9 months in a 75-year-old man with an adenocarcinoma of the cardia. In this case, there is diffusely abnormal mucosa with a pinpoint lumen through the middle. *B*, This is the barium swallow before laser treatment in the patient whose tumor is shown in *A*. There is a trickle of contrast passing through the stricture just above the top of the tube. The area around the lumen was vaporized to reveal obviously neoplastic tissue and this was shaved back with laser to reveal the tube as shown in *C*. *C*, Post-laser appearance of tube overgrowth shown in *A*. This man could swallow nothing before laser treatment, but was discharged swallowing semi-solids. His condition deteriorated fairly rapidly, but he was still able to swallow fluids when he died 8 weeks later.

it was often not possible to grip these tubes sufficiently tightly from the inside, particularly if the tumor was very hard and the tube had been in position for several months. In these cases, greater force could be applied to pull a tube up if the plastic olive of the inserter was opened below the bottom of the tube. However, if this is done the endoscopist must be prepared to remove the tube, as on one occasion, in a patient with a displaced tube (not discussed in this series), the plastic olive jammed in the bottom of the tube and could not be separated.

All patients were assessed by an experienced research nurse (M. T. or S. T.) who graded dysphagia according to a scale we have used in previous studies[1] (0 = normal swallowing, 1 = most solids, 2 = semi-solids, 3 = fluids only, 4 = difficulty with fluids). All patients were assessed before and directly following treatment while still in the hospital and subsequently by telephone. The mean dysphagia grade for each individual during follow-up was used in the analysis.

## STATISTICS

Dysphagia data were assessed using the Wilcoxon-signed rank test for paired data.

## RESULTS

Three examples of tube overgrowth are shown (Figs. 1 to 3). The 11 patients with overgrowth at the top of their tubes only were all treated with laser, but 3 also underwent tube manipulation using an Atkinson introducer following laser. The three tubes shifted were moved up to completely cover the overgrown area and further treatment was only required in one (case 1). All 11 patients swallowed a semi-solid diet for most of their survival.

Two patients with tumor distal to the tube only underwent laser treatment. One was lasered using an Olympus XQ 10 endoscope through the tube. Another was palliated by shifting the tube down with an Atkinson inserter to cover distal tumor; this uncovered tumor proximal to the tube, which was subsequently treated successfully with laser.

One patient presented with overgrowth at both ends of the tube, 18 weeks after insertion of an Atkinson tube which had allowed her to swallow semi-solids. She had relatively little tumor at the distal end. The tumor proximal to the tube was successfully treated on four occasions by laser over a period of 17 weeks during most of which time she managed a semi-solid diet. She then developed an extrinsic stricture which could not be safely treated with laser. This was dilated and a short (9-cm) Celestin tube was placed above with its bottom end impacted into the funnel at the top of the Atkinson tube. Her swallowing was satisfactory in that she managed a semi-solid diet, but this did not represent any improvement of her swallowing prior to referral with overgrowth. She died 6 weeks after the second tube was inserted.

In all, only 4 patients of the 14 studied were able to swallow fluids or better before treatment, and the rest could swallow nothing (thus, median dysphagia grade at presentation was 4). All patients except one benefited from improvement in swallowing of at least one dysphagia grade following treatment, and 10 patients by 2 clear grades. The median dysphagia grade for the survival period for each patient was calculated as in a previous study,[1] and this ranged from 0 to 3 (the median for the series was 2). The improvement in dysphagia was significant at the 1% level using the Wilcoxon-signed rank test. Improvement was achieved with only one or two endoscopies in eight patients, although, in the others, up to a maximum of five procedures were required. A median of one endoscopy was required for each 4-week survival. The median survival period was 9 weeks (range, 3 to 36 weeks). The cause of death was cancer cachexia in most patients (11 of 14). Another two patients suffered recurrent aspiration in addition to cancer cachexia which contributed to the cause of death. One of these had spinal chord compression. One patient died of a myocardial infarction and was swallowing well. Total hospital stay for endoscopic treatment ranged from 3 to 17 days (median, 5 days), although several patients were hospitalized for longer periods for social reasons or transferred for hospice care. No perforations or other serious complications were encountered.

## DISCUSSION

Laser treatment with esophageal prostheses in situ has been shown to be safe for most tubes. Mousseau-Barbin tubes can, however, ignite, and if laser treatment is essential we would recommend carbon dioxide to cool the fiber tip when treating patients with these tubes.[6] We have treated several patients with such tubes which have displaced, and to date have had no problems. Atkinson and Celestin tubes do not ignite, and it is quite safe to use air for cooling in patients with such tubes in situ.

Ethanol-induced tumor necrosis has been used to good effect in palliation of inoperable esophageal cancer,[7] and other thermal methods, such as the bipolar probe are also effective, although only recommended for circumferential tumors.[8] These techniques may also be useful for overgrowth, but we do not have experience with them. The main advantage of laser is the ability to vaporize tissue, resulting in an immediate improvement in the lumen, which in turn allows instant access to and thus treatment of tumor beyond the area first treated. This results in an immediate improvement in swallowing. It is likely that the other techniques mentioned would also be effective in this group of patients, but swallowing may only improve slowly as necrosed tissue takes a few days to slough. More treatment sessions may also be required to achieve the same result. We would, therefore, advocate the use of a Nd:YAG laser if available.

It is only recently that we have attempted tube manipulation after laser treatment. Shifting tubes which have been in position for several months require caution, as perforation is a definite risk. It is not possible to be certain of the distance between the lower end of the tumor and the bottom of the tube, and so there is always a risk of uncovering tumor at the bottom end of the tube which may be more difficult to laser.

We successfully shifted tubes in four patients who had short overgrown areas. Despite this, we feel that tube manipulation is inappropriate for most of these patients. This is because the prognosis is such that laser alone will usually provide good palliation without the necessity for multiple treatments, and without the potential risks of tube manipulation. Overgrown areas are usually too narrow to allow easy passage of the Atkinson inserter, and even in patients where this is possible, it is likely that tumor debulking with laser prior to manipulation will reduce the risk of perforation. Thus, an attempt at tube manipulation will usually involve repeated procedures that are difficult to justify in most cases.

There was one patient who underwent tube manipulation who could potentially have benefited from insertion of a longer tube. He had an overgrowth at the bottom of the tube which was shifted down to reveal tumor at the top end which was treated with laser. He swallowed semi-solids after treatment.

Two of the patients in this series had tubes inserted surgically, which were sutured in place. This would have made proximal shifting impossible (although downward displacement can still occur). It is important that this information is available to the endoscopist treating tube overgrowth, as an attempt to shift such a tube proximally could be disastrous. It is now only rarely necessary for tubes to be inserted surgically, as endoscopic techniques and equipment continue to improve. However, even if laparotomy is required, surgeons should be requested not to fix tubes with sutures as this severely limits the endoscopic options if complications arise later.

These results confirm the safety of laser treatment in patients with tubes in situ and validate an aggressive treatment approach in most of these patients. The majority of those presenting with tube overgrowth have been well palliated for surprisingly long periods, and when the overgrown area is treated with laser, swallowing is usually as good as that prior to overgrowth (usually dysphagia grade 2). The overgrown segment is mostly a short (median length 3 cm in this series) proliferative narrowing, which is easily amenable to laser treatment, and these results are usually achieved with one or two procedures.

## ACKNOWLEDGMENT

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# Radiation enhancement of laser palliation for advanced rectal and rectosigmoid cancer: a pilot study

I R Sargeant, J S Tobias, G Blackman, S Thorpe, S G Bown

**Abstract**

**Laser palliation for advanced rectal or rectosigmoid cancer requires repeat treatments every four to six weeks. Thirteen patients (seven men, six women) age range 65–91 (median 81) received additional external beam radiotherapy in an attempt to reduce the frequency of laser treatments required. After successful laser recanalisation, patients were treated with a dose of 30–55 Gy in 10–20 fractions. Bowel symptoms were well controlled for prolonged periods in 11 patients (85%) and further laser procedures were only required every 19 weeks median (range 6–53 weeks). The laser energy required after radiotherapy was only 800 J/month (median). Survival was 14 months (median, range 2·5–20 months) for the seven patients who have died. Seven patients received laser treatment only for three months or more (median 14 weeks, range 13–39). In this group control of symptoms required procedures every four weeks (median) before radiotherapy and 20 weeks (median) afterwards. The laser energy required before radiotherapy was 15 000 J/month and 2000 J/month afterwards (Wilcoxon rank sum test, p<0·01 for both). Radiotherapy was well tolerated in all but one patient. Three patients developed strictures after radiotherapy but all were dealt with endoscopically. There were no complications solely due to endoscopic procedures. Additional radiotherapy enhances laser palliation for inoperable rectal or rectosigmoid cancer.**

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The treatment of choice for rectal and rectosigmoid cancer is complete surgical resection. Unfortunately many patients present with tumours too extensive to resect or they are unfit for such surgery. The proportion of patients in this group varies between studies but is over 10%.[1 2] A further group with anastomotic recurrences are often unsuitable for further surgery. Palliative resection carries a high morbidity and a mortality of 10–30%.[1 2] The survival after palliative surgery is limited; one study[3] found a median survival of only eight and 14–16 months in such patients with and without liver metastases. A recent review[4] advises that surgeons should treat surgically incurable patients with local methods only, which are both cost effective and carry a low morbidity and mortality. Nd YAG laser treatment for inoperable rectal and rectosigmoid cancer offers good palliation.[5–9] Troublesome symptoms such as bleeding, discharge, tenesmus, and constipation (due to partial obstruction) can be controlled in most patients with minimal morbidity. One study[10] reported less satisfactory results although these may be at least partly explained because patients were not brought back as often for follow up treatments as in other studies. Repeat sessions every four to six weeks are required for good control of symptoms. This is not surprising as the Nd YAG laser is only capable of safely treating intraluminal tumours. Treatment debulks the tumour and has an immediate beneficial effect on bleeding and discharge but disease is left in the rectal wall and beyond the lumen in local nodes so tumour regrowth occurs fairly rapidly. Radiotherapy, however, has the potential for treating the entire tumour and local regional draining sites and thus should be complementary.[11] It has an established record in the treatment of rectal cancer and is commonly used as adjuvant treatment after operation for Dukes B and C cancers. The risk of local recurrence in this setting is reduced and a randomised MRC trial looking at survival is presently in progress.[12] Results from the first major series of patients treated by radiotherapy alone for rectal cancer were published in 1956.[13] Symptomatic palliation was achieved in most patients but complications were common. Half of the patients required colostomies either due to obstructive symptoms before radiotherapy or from radiation induced fibrosis. Since that time there have been several studies with more modern radiotherapy techniques and fractionation to minimise complications and maximise symptom control for advanced cancers.[14–16] Although symptoms can be controlled in most patients it takes several weeks for maximal effect and prolonged relief requires higher radiation dose regimes. These carry a higher risk of complications such as radiation swelling or fibrosis, which can in turn lead to obstruction and may even require permanent colostomy. By laser treatment and radiotherapy we aimed to achieve the benefits of both while minimising complications. Laser treatment can offer rapid relief of rectal discharge and obstructive symptoms, which should reduce the risk of obstruction from radiation induced swelling or fibrosis. Radiotherapy often relieves pain that is untreatable with laser, and may give better long term control so that repeat laser procedures are required less often. A recent pilot study with combined laser treatment and radiotherapy in oesophageal cancer[17] produced promising results. Here we present the results of a prospective pilot study of combination laser and radiotherapy for palliation of advanced rectal cancer.

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## Patient and methods

PATIENT SELECTION

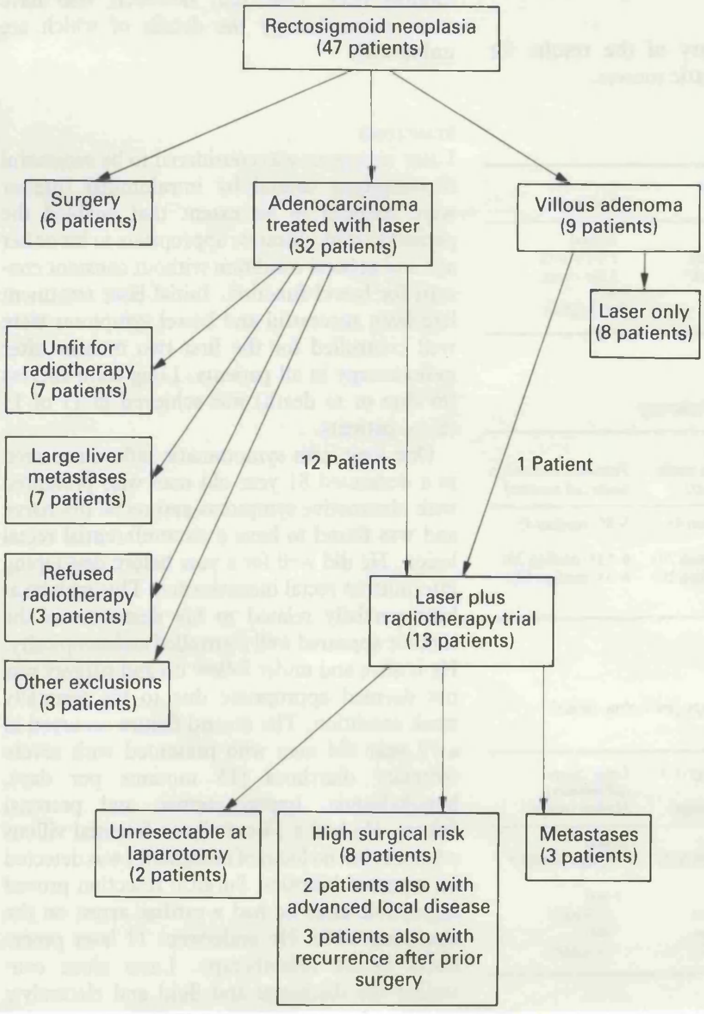
Forty seven patients with rectal and rectosigmoid tumours referred for laser treatment during an 18 month period between February 1990 and August 1991 were considered for inclusion in this study. All patients had been considered unsuitable for surgery either due to incurable disease (documented distal metastases or advanced locoregional disease), or high surgical risk such as advanced age or severe cardiorespiratory disease; 80% were tertiary referrals. The figure gives a detailed breakdown of patients included and excluded from the study.

After further assessment six patients were considered to be inappropriate referrals and were returned for surgery (two total obstruction, one tumour invading anus, three fit for surgery and resectable by anterior resection). A further eight patients with villous adenomas but no evidence of malignant change were deemed unsuitable for the study and were given laser treatment only.

Of 32 patients with proved cancer given laser treatment 12 (38%) were entered into the study. Reasons for exclusion in this group were large liver metastases (seven), carcinoma but considered unfit for radiotherapy (seven, including two sigmoid lesions), refusal of radiotherapy (three), previous radiotherapy (one), rectovaginal fistula (one), unable to pass stricture (thus radiotherapy likely to induce obstruction) (one). Thirteen patients (seven men, six women) age range 65–91 (median 81) were considered suitable for radiotherapy by the radiotherapist (JST) after a good initial laser result. All these patients had presented with rectal discharge or bleeding, nine also had diarrhoea and two had obstructive symptoms. Two also had tenesmus.

Eleven of these patients had rectal or rectosigmoid adenocarcinoma (including one with cancerous change in a villous adenoma), one had direct rectal invasion from cervical cancer, and one an extensive villous adenoma (with no documented focus of adenocarcinoma). Eleven were considered unfit for surgery including three with metastases and three recurrences after surgery, two of whom had rectal stump recurrences after abdominoperineal resections. The other two tumours were unresectable at laparotomy. The tumour length was 2–14 cm (median 5 cm) and the lower margin of the tumour was at 0–14 cm (median 6 cm) from the anal verge. At least six patients with lesions less than 7 cm from the anal margin would have required permanent colostomy if palliative resection had been carried out. Eight patients had circumferential lesions (C3) and five had ⅓–⅔ circumferential lesions (C2).

*Flow chart: all referrals with rectosigmoid neoplasia.*




ENDOSCOPIC TECHNIQUE

Whenever possible treatments were performed on an outpatient basis. A sodium phosphate enema is usually adequate preparation for rectosigmoid lesions; more proximal lesions required rectal washout or occasionally full bowel preparation. The technique is as for treating oesophageal cancers and has been published previously.[9]

RADIOTHERAPY

All patients were irradiated by supervoltage teletherapy (cobalt 60). The target volume was generally determined by computed tomography scanning and, if necessary, barium studies and treatment was delivered with anterior and posterior opposed fields in all cases. Dosage was decided on the basis of the patient's general condition, more radical regimes being offered to the younger and fitter patients. Ten received a dose of 30 Gy in 10 fractions and one patient was retreated with the same dose when rectal discharge recurred after nine months. One patient received 40 Gy in 20 fractions and a further two patients received doses of 50 and 55 Gy in 20 fractions. All treatments were given on consecutive days (weekends excepted).

PATIENT FOLLOW UP AND EVALUATION

Ten patients underwent check sigmoidoscopy three to six weeks after radiotherapy was completed. Response to radiotherapy was assessed and further laser treatment performed if a viable tumour was identified. Three patients did not return for a check as they were free of symptoms. Patients with little or no residual intraluminal tumour and a good lumen (implying minimal risk of obstruction) were not given a further follow up appointment. Those with tumour regrowth requiring laser energy of around 5000 J or more and those with a stricture that would not immediately allow passage of an endoscope were given a follow up appointment at four to six weeks for repeat laser endoscopy. This was essential because if there is a possibility of obstruction developing it is inappropriate in this patient group to wait for symptoms to develop. Inevitably, follow up appointments were given to some extent on a subjective basis according to the laser endoscopist's previous experience. As all these procedures were carried out by two endoscopists (IRS and SGB) we do not consider that this led to significant bias. All patients were subsequently contacted monthly by the research nurse (ST) to document progress and assess the necessity for further treatment. Patients were evaluated according to endoscopic result, early and late functional success, necessity for repeat endoscopic treatment, and dose rate of laser energy required to control intraluminal tumour (averaged laser energy per month).

STATISTICAL METHODS

Paired data for laser energy per month required and for frequency of endoscopic treatment before and after radiotherapy were analysed with the Wilcoxon signed rank test.

## Results

Table I gives a summary of the results for endoscopic and symptomatic success.

TABLE I *Endoscopic and symptom results*

| | *C2 tumour (n=5)* | *C3 tumour (n=8)* | *All tumours* |
|---|---|---|---|
| Endoscopic result at check | 3 Good<br>2 No check | 5 Good<br>2 Strictures<br>1 No check* | 8 Good<br>2 Strictures<br>3 No check |
| Early functional success | 5/5 | 8/8 | 13/13 |
| Late functional success | 5/5 (100%) | 6/8 (75%) | 11/13 (85%) |

*This patient benefited from late functional success.

TABLE II *Treatment interval data in weeks before and after radiotherapy*

| | *Treatment invervals in weeks (C2 tumours)* | *Treatment intervals in weeks (C3 tumours)* | *Treatment intervals in weeks (all tumours)* |
|---|---|---|---|
| Pre-DXRT (7 patients followed up for >3 months before DXRT) | 6–8 (median 7) | 3–4 (median 4) | 3–8* (median 4) |
| Post-DXRT (7 patients as above) | 20–41 (median 39) | 6–53 (median 20) | 6–53* (median 20) |
| Post-DXRT procedure interval (all 13 patients) | 9–14 (median 19) | 6–53 (median 10) | 6–53 (median 19) |

*p<0·01, Wilcoxon signed rank text.
DXRT=Deep x ray therapy.

TABLE III *Laser energy requirements before and after radiotherapy (excluding initial recanalisation)*

| | *Laser energy (C2 tumours) Median (range)* | *Laser energy (C3 tumours) Median (range)* | *Laser energy (all tumours) Median (range)* |
|---|---|---|---|
| J/month pre-DXRT (7 patients followed up for >3 months prior to DXRT) | 5000 (2500–13 000) | 22 000 (5000–26 000) | 15 000 (2500–26 000)* |
| J/month post-DXRT (7 patients as above) | 500 (0–800) | 3 500 (0–8000) | 2 000 (0–8000)* |
| J/month post-DXRT (all 13 patients) | 0 (0–800) | 2 000 (0–8000) | 800 (0–8000) |

*p<0·01.

ENDOSCOPIC DATA

All patients seen for check endoscopy had good control of symptoms at that time. Eight had minimal or no tumour present at endoscopy and the endoscope passed through the stricture with no difficulty. (None of these patients required more that 2000 J laser treatment at this time.) In this group further procedures were performed when recurrent symptoms occurred (median every 20 weeks, range 6–42 weeks). The remaining two patients had tight strictures with obvious tumour shrinkage. The stricture was clearly infiltrated with tumour in both these patients and further laser therapy was required in order to pass the endoscope above the level of the stricture. These two required regular follow up to prevent them obstructing. They had procedures on average every 10 weeks for a follow up of 15 and 16 months to death. (One with liver metastases and one tumour cachexia).

Three patients declined to come for a check endoscopy immediately after radiotherapy as they had no bowel symptoms. Two of them never required further endoscopy as their local bowel symptoms remained well controlled (survival 2·5 and 14 months). The third, a 69 year old patient with an inoperable rectosigmoid cancer, underwent further laser treatment 10 months after radiotherapy when she developed recurrent rectal discharge. This was controlled with 5000 J laser energy after which the patient had no further rectal symptoms to death six months later. (She did, however, also have some chemotherapy the details of which are unknown).

SYMPTOMS

Laser treatment was considered to be successful if symptoms caused by intraluminal tumour were reduced to an extent that enabled the patient to lead a lifestyle appropriate to his or her age and general condition without constant concern for bowel function. Initial laser treatment had been successful and bowel symptoms were well controlled for the first two months after radiotherapy in all patients. Long term success (to date or to death) was achieved in 11 of 13 (85%) patients.

One long term symptomatic failure occurred in a demented 81 year old man who presented with obstructive symptoms and rectal discharge and was found to have a circumferential rectal lesion. He did well for a year before developing intermittent rectal incontinence. This may be at least partially related to his dementia as the tumour appeared well controlled endoscopically. He is alive and under follow up and surgery was not deemed appropriate due to his generally weak condition. The second failure occurred in a 77 year old man who presented with severe secretary diarrhoea (15 motions per day), hypokalaemia, hyponatraemia, and prerenal failure. He had a 14 cm circumferential villous adenoma but no focus of malignancy was detected on repeated biopsies. Surgical resection proved impossible after he had a cardiac arrest on the operating table. He underwent 11 laser procedures before radiotherapy. Laser alone controlled the discharge and fluid and electrolyte loss and the tumour length shrank from 14 cm to 8 cm. Laser procedures were required, however, every four weeks. Initially symptoms were well controlled after radiotherapy but the mucus discharge became troublesome again after two months. The patient was reluctant to have further surgery but eventually agreed. The second procedure went smoothly (as the fluid and electrolyte problems remained controlled after laser and radiotherapy treatment), an abdominoperineal resection was performed and the patient remains well six months later. Histology of the surgical specimen showed no cancer.

### TREATMENT REQUIREMENTS

Whenever possible laser and radiotherapy were performed on an outpatient basis although many patients came from long distances so radiotherapy had to be given as an inpatient. Days in hospital ranged from nil to 52 (median 20 days). Overall the number of laser treatments required ranged from zero to 20 (median five). The number before radiotherapy was one to nine (median two) and after radiotherapy nil to 11 (median three). Table II shows the laser treatment intervals required to control symptoms. The treatment intervals before radiotherapy are given for the patients who were followed up for three months or more while undergoing laser treatment. This period was chosen as we considered that it was the minimum required to obtain a good baseline for treatment frequency and laser energy requirements for good tumour control. The initial treatment intervals start from the time of completion of the initial recanalisation, whether this took one or more treatments. Some patients were brought back routinely four weeks after recanalisation and most four to eight weeks after radiotherapy. The routine checks distort the data to some extent but because checks were performed both before and after radiotherapy the bias is minimised. The figures show a dramatic increase in treatment interval from four weeks before treatment to 20 weeks after, the treatment interval for C2 tumours being longer than that for C3 ($p<0{\cdot}01$). In terms of laser energy required to control symptoms (excluding initial recanalisation (Table III)) there was also a dramatic reduction in the figures per month required before and after radiotherapy indicating a corresponding reduction in the regrowth rate of intraluminal tumour bulk ($p<0{\cdot}01$).

### SURVIVAL AND COMPLICATIONS

To date 7 of 13 (54%) of the patients in this study have died; survival in this group was 2·5–20 months (median 14 months). Six patients are still alive and have been undergoing treatment for 5·5–24 months (median 15 months). No serious endoscopic complications occurred. Radiotherapy was generally well tolerated. One patient suffered with transitory lethargy during treatment, which may have been related to radiotherapy. Three patients developed fibrous or neoplastic strictures after radiotherapy. All were dealt with endoscopically. One, in a 91 year old woman with inoperable rectal cancer, was particularly tight and required follow up laser treatment every six weeks. She eventually died after 65 weeks of successful treatment, with severe cachexia and large bowel obstruction. At the end, her general condition was considered to be too poor to justify a defunctioning colostomy.

## Discussion

Laser treatment is now established in many units for palliation of symptoms in patients with inoperable rectal cancer. It is effective in 80% and is a particularly gentle and safe treatment not requiring general anaesthesia and carries a low risk of serious complications.[9] The problem of the need for frequent follow up procedures is, however, a major one as this is inconvenient and sometimes distressing for the patient. Laser treatment can be technically difficult, particularly in patients in whom the endoscope will not pass the stricture. It usually takes longer than with oesophageal tumours and constitutes a considerable workload. This small pilot study shows promising results for the combination of laser and radiotherapy rectal and rectosigmoid cancer. The treatments should be complementary, laser treatment to give rapid relief of troublesome discharge and obstructive symptoms and radiotherapy to attack the entire tumour bulk, and this seems to be confirmed. Also, endoscopic treatment has the advantage of pre-emptying the obstruction that may result from radiotherapy. Both endoscopic and symptomatic results were impressive.

Only two patients in this study failed to achieve long term functional success. The patient with a villous adenoma had a very extensive lesion which was initially 14 cm long and it was a notable success to control his troublesome rectal discharge at all. Even he had definite symptomatic and endoscopic benefit from additional radiotherapy and his general condition improved enough for him to undergo successful surgery. The reduction in follow up procedures to one every 20 weeks or so for C2 tumours and 10 weeks or so for C3 tumours is a useful improvement in follow up requirements.

The reduction in laser energy per month required for good symptom control is another indicator that suggests benefit from radiotherapy. Only 12 of 32 patients referred with rectal or rectosigmoid cancer who received laser therapy during the 18 month period were entered into this study. We were reluctant to submit patients with very poor prognosis to a two week course of radiotherapy and the small proportion entered reflects the extent of disease and poor general condition in this elderly group who are referred for laser treatment. The median survival of a year or more with symptoms controlled in most of those treated represents a very satisfactory outcome. Despite the development of radiation strictures in three patients none required open surgery. All were controlled for long periods with endoscopic treatment although it is possible that obstruction contributed to death in one patient.

There are several other treatments available for palliation of rectal and rectosigmoid cancer;

these include electrocoagulation,[19] transanal resection,[20] and cryotherapy.[21] They are all more aggressive than treatment with laser and carry a higher risk of complications and only cryotherapy can be performed without general anaesthesia. All of these treatments, however, suffer from the same inability to reach tumour outside the bowel wall. It is likely that a combination of these modalities with radiotherapy might also be complementary. To further clarify the benefit of the combination of topical techniques for tumour destruction and external beam radiotherapy randomised studies are required.

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;ASTROINTESTINAL ENDOSCOPY


# Cuffed esophageal prosthesis: a useful device in desperate situations in esophageal malignancy

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**Sixteen patients (three groups) underwent endoscopic intubation with cuffed Wilson-Cook esophageal endoprostheses. Group 1 comprised 10 patients with spontaneous esophago-respiratory fistulas due to malignancy. Six primaries were esophageal, three bronchial and one ovarian. One patient could not tolerate a cuffed tube. All other fistulas closed with intubation but two tubes displaced later. Seven patients managed a soft diet after intubation, but two liquids only. Median survival was 4 weeks (range, 0 to 9 weeks). Group 2 comprised three patients with large endoscopic instrumental tears. Two had definite perforations with extensive surgical emphysema. All had satisfactory contrast swallows the day after intubation and were started on semi-solid diets; median survival was 10 weeks (one still alive). Group 3 included three patients with life-threatening arterial bleeding from cancers of the gastric cardia. No further bleeding occurred in any of the three after intubation and two survived for extended periods (15 and 26 weeks). Cuffed tubes are invaluable in these desperate situations and are worth considering for symptomatic relief even when prognosis is short. (Gastrointest Endosc 1992;38:669–675)**

Following a favorable report using Ivalon sponge wrapped around an Atkinson tube for malignant esophago-respiratory fistulas,[1] the "cuffed" tube was designed exclusively for this purpose. These fistulas present a difficult and distressing complication of mediastinal cancer which untreated, is rapidly fatal. Presentation is often acute and is manifested by severe bouts of coughing when food or fluids are taken by mouth and by recurrent pulmonary infection and collapse. There have been case reports[2-5] of satisfactory treatment of fistulas with the cuffed prostheses, but no more than two patients are included in each.

At our laser center, we are palliating 150 new patients a year with esophageal cancer and the occasional patient with direct spread from carcinoma of the bronchus or secondary cancer involving the esophagus. Most of our patients (80%) are tertiary referrals, and thus one would expect a high level of complicated or difficult cases. We first obtained cuffed Wilson-Cook esophageal endoprostheses (William Cook Europe Limited) in early 1990 and in 2 years since we have used them in the 16 cases described. This represents 5.3% of all cases. Ten (3.3%) had esophago-respiratory fistulas which is in the same order (3 to 5%) as reported in other series.[1,5] In addition to treatment of this group of patients, we have found these tubes to be invaluable in certain difficult, if not desperate, situations in esophageal malignancy which are described.

## MATERIALS AND METHODS

The prosthesis (Fig. 1A) is a standard Wilson-Cook silicone rubber tube containing a metal coil with soft silicone rubber ends. The cuff is formed by a layer of foam rubber wrapped around the shaft of the tube which is surrounded by a thin sheath of silicone rubber. The foam inside the cuff will self-inflate if allowed. It is deflated immediately prior to insertion (Fig. 1B) by means of a plastic cannula which inserts into the cuff and is attached to a 50-ml syringe.

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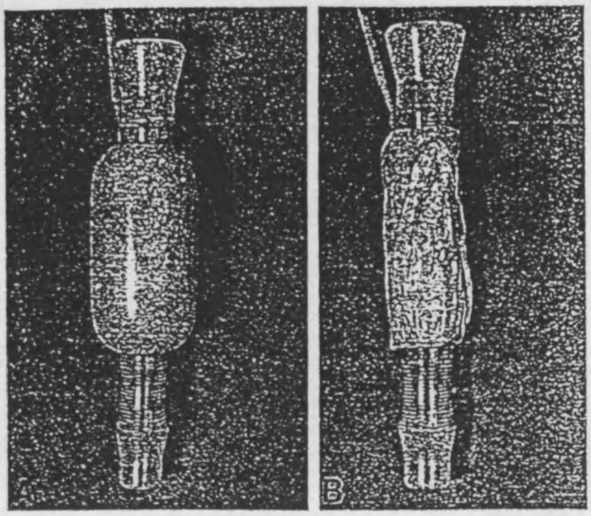

Figure 1. *A*, A 10.4-cm (shaft) Wilson-Cook cuffed tube with the cuff inflated is shown. *B*, The same tube is shown with the cuff deflated ready for insertion.

When satisfactorily positioned with the fistula at the midpoint of the cuff, the balloon can be inflated with air before the cannula is pulled out of the cuff prior to freeing of the tube from the introducer. The cuff will, however, self-inflate once the cannula is removed, and we have found that inflation with a syringe is not really necessary (and may cause respiratory distress—see Results and Discussion). The soft foam contours the shape of the esophagus once in situ to a maximum diameter of 36 mm (deflated diameter of 23 mm). The tubes come in several lengths but the cuff is located at the top of the shaft and is positioned the same distance from the top of the tube (3 cm approximately) for all sizes. All tubes have a soft funnel at the proximal end which is 2.5-cm long and a distal funnel (to help stop upward displacement) which is 2-cm long. The tubes are sold according to shaft length (4.4 to 16.4 cm in 2-cm increments) and thus the total tube length is 4.5 cm longer than this.

Patients are intubated under sedation using endoscopic and fluoroscopic control. Transcutaneous $pO_2$ monitoring is routine. The esophagus is usually dilated to 18 mm with Celestin dilators prior to tube insertion; some patients with fistulas do not have strictures, in which case dilation is not performed. We use an Atkinson introducer to place these tubes which grips them nicely and saves the expense of an additional Dumon-Gilliard introducer, which has been recommended for insertion. Extra care is required when endoscoping these patients as secretions and debris in the esophagus can easily enter the airways and cause respiratory distress. It is important to suction such secretions with the endoscope before this occurs. It is also advisable to have sedation-reversing agents readily available should they be required. One patient developed acute respiratory distress shortly after intubation with a cuffed prosthesis which had to be removed. This can occur with conventional prostheses (particularly when used for tumors of the cervical esophagus), but this may be more likely to happen with a cuffed tube as it is possible for the cuff to protrude through the fistula and obstruct the involved bronchus. It is thus important that there is a coordinated team approach with appropriate equipment available to rapidly remove the tube if necessary.

## RESULTS

### Group 1: esophago-respiratory fistula

All patients with fistulas are documented in Table 1; nine fistulas occurred in the thoracic and one in the cervical esophagus. All patients had difficulty swallowing fluids prior to intubation. Ten patients with esophago-respiratory fistulas were considered suitable for cuffed tubes. Seven fistulas were demonstrated radiographically, one of which (case 7) could not be seen at endoscopy. The other three (cases 3, 4, and 6) were demonstrated at endoscopy only and cuffed tubes were inserted at the same procedure. Only one patient (case 9) had not undergone radiotherapy or laser treatment prior to the development of a fistula and three patients had received both.

Success was deemed as the abolition of coughing with swallowing, confirmation of fistula closure with a contrast swallow and the ability to take a soft diet for the remaining survival period. Using these criteria, five cases were regarded as completely successful and five cases were only partially successful. One of these partial successes was only achieved with a standard Celestin prosthesis as the patient developed acute respiratory distress after cuff inflation and the cuffed tube had to be removed. Two of these patients who initially did well suffered a recurrence in symptoms from tube displacement, one tube kept slipping despite two attempts at repositioning (case 4) and the other patient suffered a perforation when the tube was replaced (case 2) and died. One patient was only able to swallow fluids despite closure of the fistula and another died of bronchopneumonia (established prior to the procedure) 48 hours following the procedure after swallowing fluids only.

*Case report A(esophageal primary).* A previously well 61-year-old man presented with dysphagia and was found to have a squamous cell carcinoma at 25 to 30 cm from the incisors (mid-thoracic lesion). A CT scan showed thickening of the esophageal wall on the right anterolateral aspect from just below the level of the sternoclavicular joints to the level of the carina. The mass was contiguous with the posterior aspect of the trachea and the anterior aspect of the aorta and was thus thought to be unresectable. He was referred for radiotherapy and received a dose of 60 Gy in 20 fractions over 4 weeks. Dysphagia improved during this period enough to allow some solid food to pass but after an additional month his swallowing deteriorated again and he was referred for laser treatment. Over the following 15 weeks swallowing was excellent with dilations and laser for a combined intrinsic/extrinsic stricture (three procedures). The patient

**Table 1.**
**Patients with fistulas**

| Patient | Nature | Histology | Sex | Age | Previous radiotherapy | Previous laser | Tumor level from incisors (cm) | Fistula (cm) | Success | Survival | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Esophageal | Squamous | M | 61 | Yes, 60 Gy | Yes, 3 treatments | 25–30 | 25 | Yes | 9/52 | Case report A |
| 2 | Ovarian | Adenocarcinoma | F | 62 | Yes, 30 Gy | Yes, 2 treatments | 25–30 | 27 | Partial | 4/52 | Case report B |
| 3 | Esophageal | Squamous | M | 48 | Yes, 45 Gy | No | 26–40 | 38 | Yes | 3/52 | 2 fistulas, previous celestin tube ineffective |
| 4 | Esophageal | Squamous | M | 69 | No | Yes, 3 treatments | 23–27 | 25 | Partial, 3/52 | 6/52 | Tube slipped and could not be repositioned |
| 5 | Esophageal | Squamous | F | 49 | Yes, 30 Gy | Yes, 3 treatments | 20–25 | 21 | Partial | 4/52 | Only swallowing fluids |
| 6 | Esophageal | Squamous | F | 81 | Yes, 20 Gy | No | 20–28 | 25 | Yes | 13/52 | Schizophrenic |
| 7 | Bronchial | Anaplastic | M | 51 | Yes, 20 Gy | No | 30–50 | Not seen | Yes | 2/52 | Fistula only demonstrated with radiology |
| 8 | Bronchial | Squamous | M | 57 | Yes, 30 Gy | No | 29–35 | 30 | No | 48 hr | Died of bronchopneumonia 48 hr after procedure |
| 9 | Bronchial | Non-small cell | M | 62 | No | No | 23–29 | 23–29 | Yes | 6/52 | |
| 10 | Esophageal | Squamous | F | 57 | Yes, 60 Gy | No | 20–25 | 20 | Yes, with Celestin tube | 2/52 | High fistula, respiratory distress with cuffed tube |

then developed coughing on swallowing liquids and was found to have an obvious fistula at the top end of the tumor at 25 cm from the incisors. A 15-cm Celestin tube was placed through the stricture (top at 19 cm) to cover the fistula but unfortunately a contrast swallow showed contrast was flooding around the tube and through the fistula. The Celestin tube was removed and a 10.4 cm (shaft length) cuffed tube was inserted which closed the fistula nicely. The patient was able to drink and eat some soft food. He was discharged after 10 days and lived a total of 9 weeks after cuffed tube insertion on a diet of soft food.

*Case report B (ovarian primary).* A 62-year-old woman with a 10-year history of ovarian cancer with pulmonary and mediastinal involvement and dysphagia for all but fluids was referred for laser therapy. Following surgery she had remained well for 7 years when she presented with chest metastases. She was treated with chemotherapy, but later developed an obstructed right main bronchus from tumor infiltration. This was treated with laser and intraluminal (iridium wire) radiotherapy and external beam radiotherapy to good effect. Shortly after this, some difficulty in swallowing was noted and a contrast swallow showed some narrowing and distortion of the thoracic esophagus which was thought to be due to extrinsic tumor. It was however an additional 13 months before dysphagia became an intractable problem. At referral a polypoid growth was noted from 25 to 30 cm from the incisors. This was treated at two sessions with laser and swallowing improved to allow a semi-solid diet. Two weeks after the second laser, the patient developed a fistula into the right main bronchus in the upper part of the tumor. A cuffed tube (10.4-cm shaft) was inserted with the center of the cuff at the level of the fistula. There was an immediate improvement in chest symptoms after intubation and the patient was discharged a few days later and remained well on a soft diet for 4 weeks. At that time she began to cough when taking liquids once again and the tube was found to have displaced. In addition there appeared to be extrinsic compression of the esophagus below the tube and we elected to remove it and replace it with a longer one. Unfortunately an esophageal perforation developed during this procedure and despite a nicely placed 16.4-cm (shaft) tube and full conservative treatment the patient died 24 hours later.

### Group 2: esophageal perforation/tear

In the past we have elected to intubate such patients with conventional tubes but we believe cuffed tubes may allow a more rapid re-introduction of oral intake (Table 2).

*Case report C.* An 80-year-old woman was referred with a 1-month history of dysphagia for solids. At endoscopy she was found to have a 4-cm mid-thoracic lesion which was subsequently found to be a squamous cell cancer. The stricture was tight and the endoscope would not cross. A wire was passed and the stricture was dilated under fluoroscopy, initially with the small Celestin dilator (maximum diameter 11 mm) and then with the large Celestin dilator (maximum diameter 18 mm). The large dilator was passed as far as it would go so that the stricture was fully dilated to 18 mm. In retrospect, this was too "aggressive" as following dilation the tumor was seen to have split along its full length and the pleural cavity could be seen. The patient rapidly developed subcutaneous emphysema and a cuffed tube was inserted across the perforation. Intravenous antibiotics were given for 3 days and then converted to oral for a total of 7 days. A contrast swallow 24 hours later showed no leak, but air in the mediastinum was noted. A soft diet was commenced and the patient was discharged 6 days later. She has remained well on a semi-solid diet and is alive and well 6 months later.

### Group 3: Life-threatening bleeding

Arterial spurting from tumors is not common but is occasionally laser induced as in the first two of our cases (Table 3). All of the cases treated had adenocarcinomas of the cardia. The first two were localized tumors but the third case had an extensive tumor 11 cm long. Cuffed tubes were highly effective for controlling bleeding in all cases. The first two swallowed well and lived for a prolonged period. The last case was a man with an extensive tumor who was dying. The tube, however, allowed him a peaceful demise without hematemesis and the ability to swallow liquids.

*Case report D.* A 75-year-old man with an unresectable adenocarcinoma of the cardia and aortic stenosis was referred for laser treatment following a laparotomy. He had presented with a 2-month history of

**Table 2.**
**Patients treated for esophageal perforation or tear**

| Nature | Histology | Sex | Age | Length (cm) | Perforation | Survival | Comments |
|---|---|---|---|---|---|---|---|
| Cardia | Adenocarcinoma | F | 63 | 5 | Y subcutaneous emphysema | 6/52 | Died suddenly swallowing well |
| Thoracic esophageal | Squamous | F | 80 | 4 | Y subcutaneous emphysema | 40/52+ | Alive and well on semi-solids |
| Cardia | Adenocarcinoma | F | 74 | 3 | N-tear after tube removal | 10/52 | Swallowed semi-solids until death |

Table 3.
Patients treated for life-threatening bleeding

| Tumor | Age | Sex | Laser induced? | Transfusion required | Success | Survival (wk) |
|---|---|---|---|---|---|---|
| Adenocarcinoma cardia | 84 | F | Yes, acute | 2 units in 4 hr | Yes | 15 |
| Adenocarcinoma cardia | 75 | M | Yes, initially | 11 units in 2 wk | Yes | 26 |
| Adenocarcinoma cardia | 71 | M | No | 4 units in 1 wk | Yes | 1 |

dysphagia and weight loss and was found to have a large tumor at the cardia. At laparotomy the tumor mass was found to be arising from the lower esophagus and was firmly fixed posteriorly. There were also tumor nodules in the gastro-hepatic omentum and thus no attempt at resection was made. Initial laser recanalization for a predominantly polypoid tumor (38 to 41 cm from the incisors) was performed in a total of five sessions due to the large tumor bulk. An excellent lumen was achieved and the patient was able to manage most solids. Swallowing remained excellent with monthly laser treatments and the patient remained remarkably well. Three months later at a routine laser treatment fresh blood was found in the stomach and an arterial spurter was identified at endoscopy at 40 cm from the incisors (tumor 35 to 42 cm). Bleeding was stopped with laser and injection of 8 ml of 1:10,000 adrenaline. Following a 4-unit blood transfusion the patient was discharged. One week later, he had a severe episode of hematemesis and melena and was admitted to a local hospital in shock with a hemaglobin of 4. Five units of blood were transfused and he was transferred back to us after another week. At that time further active bleeding was found from the same site for which an additional 3 units of blood were transfused. We elected to insert a 10.4-cm (shaft) cuffed tube with the center of the cuff at the level of the spurter. Following this procedure the patient was able to swallow a semi-solid diet. He lived another 6 months (survival from referral = 10 months) and had no further bleeding.

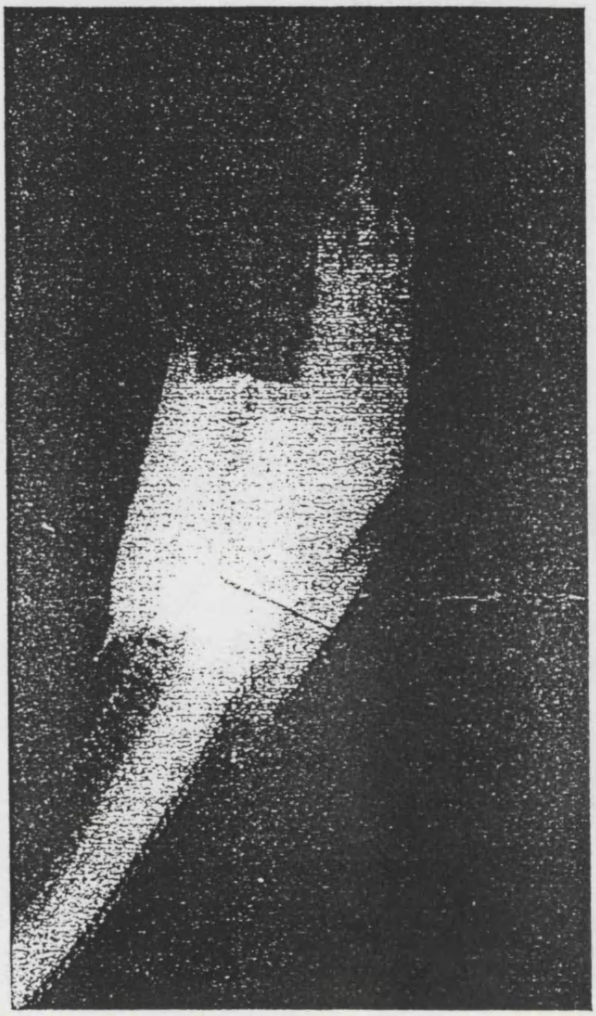

**Figure 2.** Case report 3. A cuffed tube was inserted and this contrast swallow performed afterward shows no mediastinal leak. Contrast floods around the tube and stops abruptly at the level of the cuff. Air in the partially inflated cuff can be seen.

## DISCUSSION

There are three main aims in the treatment of malignant esophago-respiratory fistulas. These are (1) to exclude esophageal contents from the respiratory tract, (2) to restore swallowing as well as possible, and (3) to carry an acceptable morbidity and mortality. Surgical management is frought with problems. A variety of surgical bypass techniques has been described using stomach or colon for interposition with a presternal or substernal approach.[6-8] This type of surgery is highly invasive and the poor general condition of these patients results in a high mortality (30 to 40%) and incidence of local complications.[6, 8] These values are not acceptable for treatment of incurable patients and hence the need for less invasive therapies. Surgical exclusion alone is one option but combined cervical esophagostomy and gastrostomy still carries a 10% mortality[8] and does not allow the patient to swallow. Endoscopic techniques are able to fulfill the three aims in the treatment of these patients. Survival in this group is limited (median 4 weeks in this series) but prolonging survival is not the main aim of treatment.

All but one of the fistulas were associated with

Table 4.
Published series of esophageal prosthesis for treatment of fistulas

| Authors | Tube | Patient no. | Success | Median survival (wk) | Comments |
|---|---|---|---|---|---|
| Robertson and Atkinson[1] | Atkinson & ISR Atkinson | Total 11; 6 At,* 5 ISR At | 8/11 (72%) | 8.5 | 1 died post-procedure, 3 fistulas not closed |
| Davidson et al.[10] | Atkinson | 6 | 4/6 (66%) | 10 | 1 died post-procedure, 1 fistula not closed |
| Buess et al.[11] | Various | Total 21 | 18/21 (85%, but 6 tubes changed) | 6 | 2 died post-procedure |
| | Eska Buess + fistula funnel | 3 | | | 1 fluids only |
| Lux et al.[2] | Cuffed WC tube | 1 | Yes | — | Case report |
| Irving and Simpson[3] | Cuffed WC tube | 2 | Both | Some | Case reports |
| Loizou et al.[12] | "Modified" Celestin | 3 (cervical) | 2/3 | 6 | 1 swallowing little |

* At, Atkinson tube; ISR At, Ivalon sponge-wrapped Atkinson tube.

previous laser or radiotherapy and this association has been noted by other authors.[9] Unfortunately, pressure necrosis from standard prosthetic tubes can also be responsible for this complication, and thus intubation of patients known to have tumor adjacent to an airway is not necessarily a way of avoiding this problem. Conventional tubes may allow ingested material to pass along the side of the tube and through the fistula (case A), and other reports have documented this problem.[3, 9] The effect of the cuffed tube is well demonstrated by Figure 2 which shows contrast passing down the side of a tube and stopping dead at the cuff. It is not uncommon for fistulas to occur in the absence of a stricture and the problem of tube migration is largely avoided with a cuffed tube in these cases.

The important published data with esophageal prostheses for fistulas[1-3, 10-12] is summarized in Table 4. In some of the publications, two or more types of tube have been used in these patients and it is difficult to determine which results have been achieved with which tubes. Authors using various modified prostheses appear to have achieved results similar to ours, although "standard" prostheses probably only close a fistula at the first attempt in about 50% of patients. The technique of Ivalon sponge wrapping[1] in 4 of the 11 tubes inserted, fully closed 8 of 11 fistulas and 10 of the patients left hospital. All but one managed a semi-solid diet. Median survival was 8.5 weeks. Another report[11] advocated a modified tube with a large upper funnel (fistula funnel) for these patients. Twenty-one patients with fistulas were studied, although only 3 were intubated with these modified tubes; 18 were "successful" but only with a tube change in 6 patients. Median survival was 6 weeks. These tubes may offer an advantage over the cuffed tube in patients with high fistulas. The problem with using a cuffed tube in this situation is that the full diameter of the cuff starts only 4 cm from the top of the tube and thus when the cuff is placed at the level of the fistula, the top of the tube protrudes into the back of the throat and may not be tolerated. We have found a similar device useful in treating high cervical lesions;[12] three of the eight patients so treated had fistulas which were sealed. However, for lesions in the thoracic esophagus, it is surprising that such an approach is effective as there is often marked esophageal dilation proximal to a stricture. A potentially disastrous problem was encountered in our patient who suffered acute respiratory distress after cuffed tube intubation. It is possible that the problem was exacerbated by cuff inflation. We have now discontinued this practice and prefer to allow the tube to self-inflate. Such problems do however underline the need for a team approach, and the ability to remove a tube at short notice in such patients.

Patients with esophageal malignancy suffering instrumental perforation at endoscopy are another problem group. In the past it has been our practice to intubate them immediately with conventional tubes, but we were very cautious in restarting oral intake, particularly in patients with long tears. We usually waited 4 or 5 days before requesting a contrast swallow. Use of a cuffed tube allows more rapid re-introduction of oral intake. All three patients had contrast swallows and were started on fluids within 48 hours of the trauma and were discharged within 1 week. Use of a tube with a "fistula funnel" would probably also suffice for such lesions. We have treated one patient with a very high perforation (1 cm below the vocal chords) with a similar tube with a large floppy funnel.[11] The perforation occurred after dilation of a tight fibrous stricture (and recurrence) consequent on prior radical radiotherapy for a squamous cell cancer. The perforation was nicely sealed with the modified tube and the patient swallowed a semi-solid diet and survived for 4 months.

Severe bleeding from esophageal cancers can be extremely difficult to control. Arterial spurters in malignant tissue often do not respond to injections or laser as well as similar vessels in peptic ulcers. Such cases present a real dilemma as to suffer recurrent hematemesis and bleed to death is a particularly unpleasant demise for patients who are often alert. The two who went on to survive several months were both bleeding severely, and might well have died from bleeding if they had not been intubated. We found cuffed tubes invaluable for these patients for whom there is no alternative.

We have found cuffed tubes invaluable in the three groups of patients discussed. Even when the prognosis is poor these tubes have something to offer both in terms of prolonging life in some cases, but equally importantly in palliating miserable symptoms and allowing a dignified death.


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GASTROINTESTINAL ENDOSCOPY


# Non-optic endosonography in advanced carcinoma of the esophagus

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**The assessment of advanced esophageal cancer with a 5-MHz steerable non-optic ultrasound probe is described. Non-optic endosonography was performed on 80 occasions in 50 patients; the probe could be passed successfully on 75 occasions. In all cases, good visualization of the extent of esophageal tumor was obtained and discrimination between the tumor mass and discrete peri-esophageal lymph nodes was possible. The technique was valuable in monitoring tumor response to laser therapy and radiotherapy, and in guiding the laser endoscopist away from areas of minimal thickening. (Gastrointest Endosc 1994;40:194-8.)**

Although endoscopy allows visualization of the esophageal lumen and the extent of esophageal cancer, it does not show the depth of tumor or any involvement of surrounding organs. Treatment of asymmetrical esophageal tumors by endoscopic laser therapy entails a risk of perforating the esophageal wall.[1] Computed tomography and magnetic resonance imaging both give indications of the extent of extra-luminal disease and involvement of surrounding organs,[2-4] but only endoscopic ultrasonography (EUS) adequately shows the distribution of primary disease and the location of peri-esophageal lymph nodes.[5-7] However, the equipment is expensive (about $150,000), and in at least 50% of advanced carcinoma cases the 13-mm-diameter fiberoptic EUS probe (Olympus/Keymed, Southend, U.K.) is not able to pass the stricture without prior dilation.[5]

The accuracy of the conventional fiberoptic EUS probe in staging esophageal cancer according to the TNM system is well documented—between 80% and 90%.[5] However, the full extent of a tumor can be assessed only after the stricture is passed. For local ablative procedures, it is important to be able to discriminate between the primary tumor and contiguous peri-esophageal lymph nodes. The EUS probe also allows visualization of the invasion of surrounding structures, such as the trachea, aorta, and pericardium, whereas their involvement can normally only be inferred with other imaging modalities.

The linear array endoluminal ultrasound probe used in this study, which was designed for trans-esophageal echocardiography, is significantly narrower than the standard EUS probe—8 mm compared with 13 mm. It is significantly less expensive (about 8% of the cost) than the fiberoptic instrument and interfaces directly with a standard Aloka SSD 650 console (Keymed, Southend, U.K.). It therefore may be suitable for widespread use in patients with stenosing esophageal carcinoma, and our experience with this probe is presented.

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## METHODS

A standard Aloka 5-MHz curved linear array probe (UST-936-5) was used in this study. Its cross-sectional shape is approximately square, with smooth contours, minimizing the risk of esophageal injury. It can be steered in one plane 5 cm from the tip by rotating a knob on the handle (Figs. 1 and 2), and can be connected via an adaptor to a standard Aloka SSD 650 ultrasound console. The probe is passed into the esophagus trans-orally (Fig. 3) after administration of local pharyngeal anesthesia with lidocaine (Xylocaine) spray and intravenous sedation with Diazemuls with or without pethidine, as in conventional side-viewing endoscopy. Patients referred to the study from this and other hospitals all had stenosing carcinoma of the esophagus that was causing

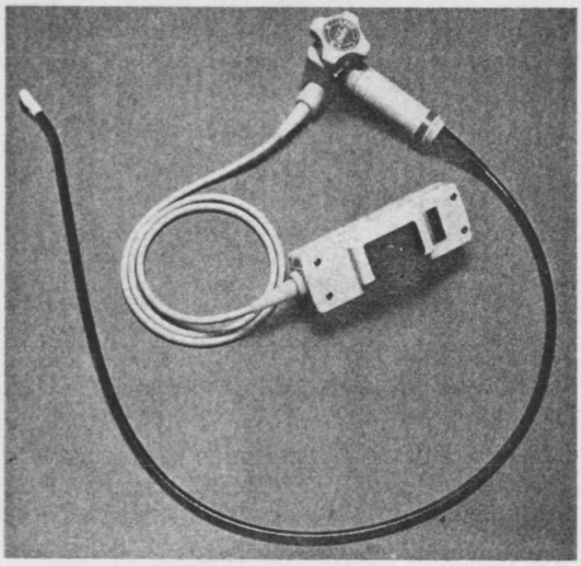

**Figure 1.** Aloka 5-MHz curved linear array probe (UST-936-5).

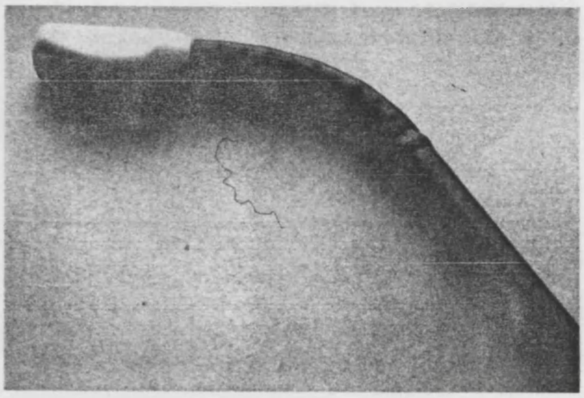

**Figure 2.** Close-up view of the curvilinear transducer showing tip deflection.

swallowing difficulty. These cases were not amenable to surgical treatment either because of advanced stage of disease or poor general state of health.

Fifty consecutive patients were included in the study (36 men and 14 women whose ages ranged from 57 to 88 years; mean age, 72 years). Thirteen patients had squamous cell carcinoma and 37 had adenocarcinoma. All the patients had previously been assessed by endoscopy before esophageal EUS, but not necessarily immediately before the procedure. The probe was steered into the esophagus using gentle pressure and tip deflection and was passed down to the level of the tumor and beyond if possible. As during conventional endoscopy, excessive pressure is to be avoided because of the risk of trauma. The technique of esophageal scanning is different from that of the radial-scanning Olympus (GF-UM3 or GF-UM20) instruments; more manipulation is required to obtain complete visualization. As balloon displacement is not available, the probe has to be pressed into contact with the esophageal wall by means of tip deflection and then rotated 360° at each level to image the extent of tumor through all four quadrants. The probe has good torque, but reference to structures outside the esophagus (e.g., aorta, heart, vertebral column) is useful to confirm which quadrant is being examined. These remain visible even in the presence of a grossly thickened esophageal wall.

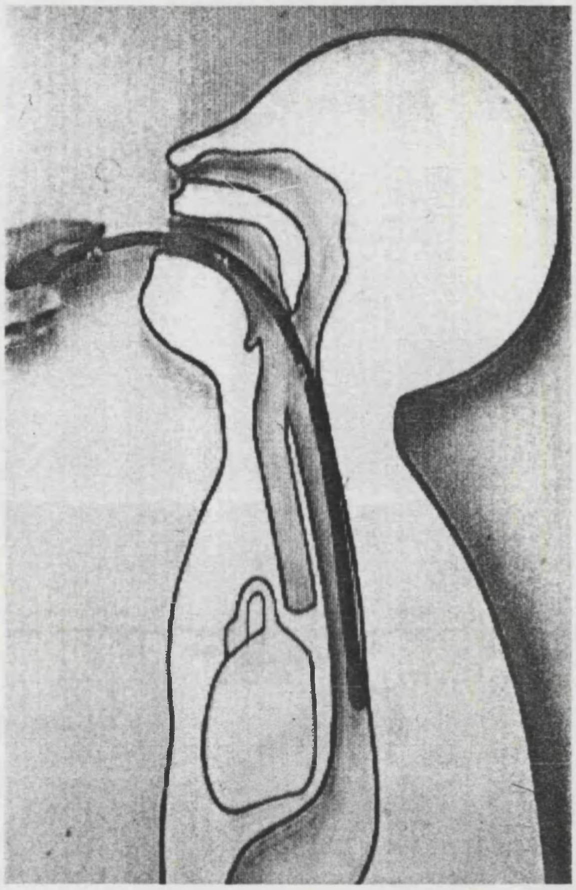

**Figure 3.** Diagram of position of probe during scanning.

## RESULTS

Esophageal EUS was performed on 80 occasions in 50 patients. The probe could not be passed into the esophagus in two instances—once in a patient with a pharyngeal pouch and once in a patient who had a high esophageal tumor just below the level of the glottis. In one case the probe was initially passed into the trachea but was removed by gentle manipulation; it did not cause respiratory embarrassment while incorrectly positioned. In all other patients the probe was passed easily into the esophagus and down to the level of the carcinoma. It was possible to manipulate the probe to the distal end of the tumor in the majority of patients, but the stenosis could not be passed on five occasions despite previous endoscopic dilation and laser treatment; three of these were investigated immediately after laser therapy. No adverse events were associated with the esophageal EUS.

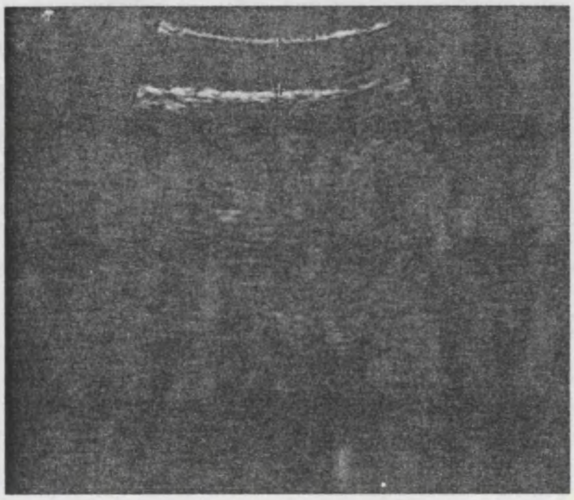

**Figure 4.** Normal esophageal wall measuring less than 4 mm easily discriminated from peri-esophageal fat.

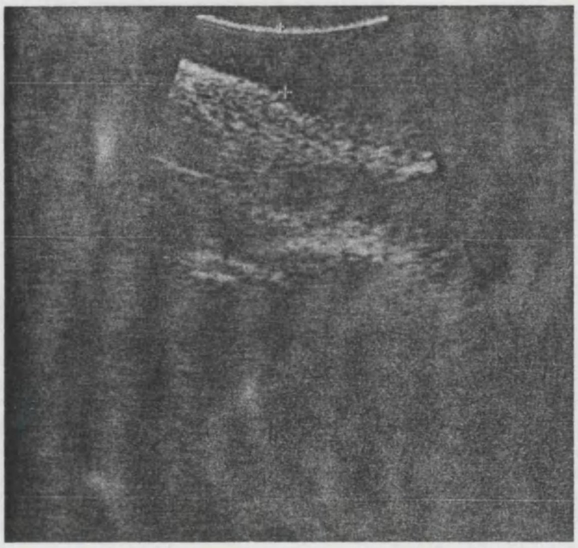

**Figure 5.** Area of transition between normal esophageal tissue *(left of markers)* and diseased, thickened esophageal tissue *(right of markers).*

Compared with the radial instrument, image resolution is worse in the near range of the transducer (i.e., within 1 cm) but significantly better in the far field (beyond 3 cm). Thus, the resolution of the 5-MHz probe was insufficient to show layers within the normal esophageal wall, although it was possible to measure the thickness of the esophageal wall and discriminate between normal and diseased esophageal tissue (Figs. 4 and 5), peri-esophageal tissues, lymph nodes (Fig. 6), and surrounding organs. With the probe positioned in the stomach, metastatic disease in the left lobe of the liver could be demonstrated (Fig. 7), although the whole of the liver was not visible. With the probe directed posteriorly, retro-peritoneal lymphadenopathy

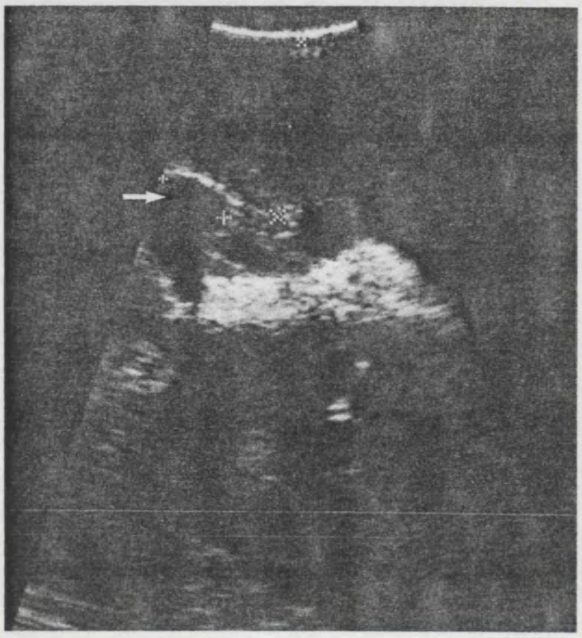

**Figure 6.** Enlarged (8 mm) lymph node lying outside thickened esophageal wall at the cardia *(arrow).* The left lobe of liver is seen at the bottom of the image.

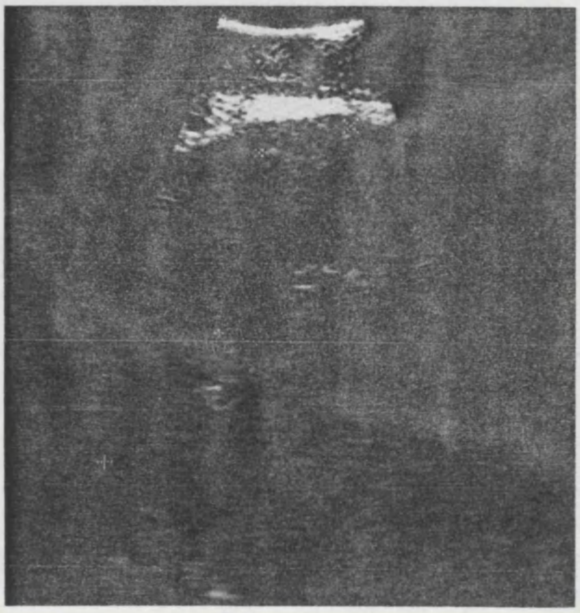

**Figure 7.** Several bright, hyper-echoic metastases *(between cursors)* scattered within the left lobe of the liver. A portal vein is seen running across the middle of the image.

could also be seen (Fig. 8). Poor contact and interposition of small gas bubbles between the probe and the mucosa occasionally caused unsatisfactory images, but this could usually be overcome by manipulating and re-positioning the probe. In a few patients it was difficult to assess mobile, soft, exophytic growths displaced by the probe, but this occurred only in a

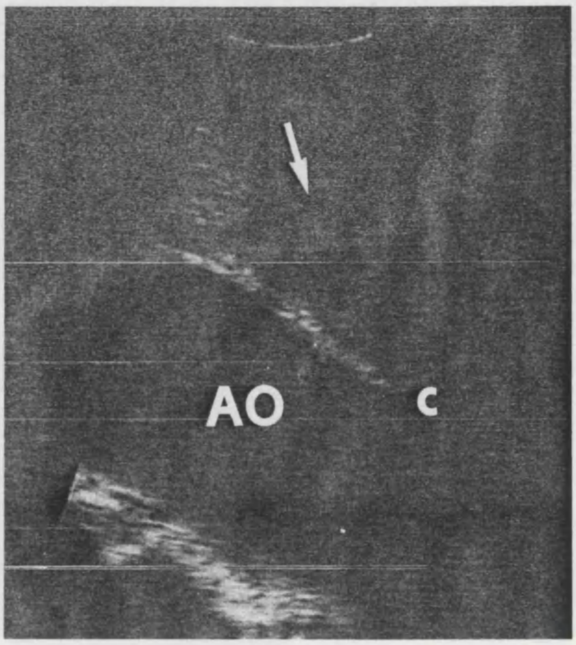


**Figure 8.** A 2-cm lymph node *(arrow)* lying superior to the celiac axis *(C)* and anterior to the abdominal aorta *(AO)*.

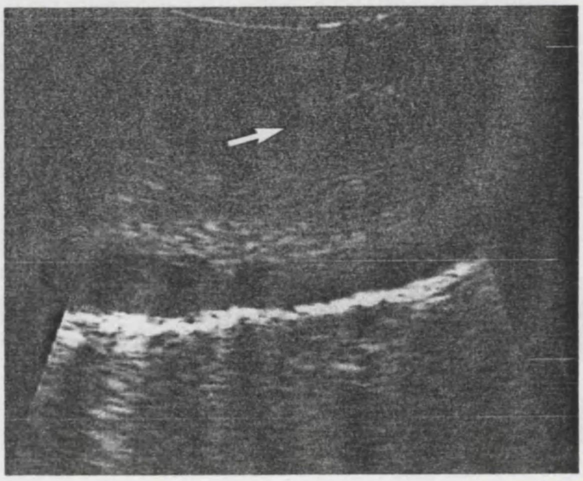

**Figure 9.** Esophageal tumor mass *(arrow)* invading a lymph node *(markers)*, pathognomonic for nodal involvement.

minority of cases. Changes were also observed within the esophageal tumor mass after laser therapy; edema is associated with reduced echogenicity, but some small internal hyper-echoic areas are also seen. We have noted this characteristic appearance shortly after laser treatment in several patients and believe that it may represent interstitial gas bubbles related to vaporization produced by the laser. Peri-esophageal lymph nodes as small as 5 to 6 mm could be identified, and direct nodal invasion, pathognomonic for nodal metastatic disease,[5] could also be demonstrated (Fig. 9).

## DISCUSSION

Most ultrasound equipment manufacturers produce probes designed for trans-esophageal echocardiography, and as use of this type of probe for EUS need involve only the additional expense of purchasing a transducer when a suitable conventional ultrasound console is already available, it provides a much less costly option than fiberoptic EUS. The 5-MHz linear probe used in this study cannot provide adequate resolution to stage early esophageal cancer, but it readily demonstrates thickening of the esophageal wall and can discriminate between this and normal areas. Higher-frequency probes of similar design may be able to resolve the layers of the esophageal wall and therefore be useful for staging, but some preliminary studies we performed with a 7.5-MHz probe showed no significant advantage. However, more than 80% of esophageal cancers in U.K. practice are at stage T3 or T4 at presentation[8]; these are most likely to be referred for conservative management. In these patients the visualization obtained using the 5-MHz probe is adequate for assessing local disease, peri-esophageal lymph node involvement, and extension of malignancy into surrounding structures and for following response to treatment. Criteria for distinguishing benign from malignant lymph nodes on EUS have already been described by Vilgrain et al.[7] Briefly, malignant nodes demonstrate one or more of the following features: they are hypo-echoic, round, well-defined, and larger than 5 mm, whereas benign nodes are hyper-echoic, poorly defined, ellipsoid or triangular, and smaller than 5 mm. Some liver metastases and enlarged abdominal lymph nodes can also be seen. We have also found this technique useful in guiding the laser endoscopist away from areas where the esophageal wall is only minimally thickened or adherent to major structures, such as the descending aorta.

The probe can easily be passed by an experienced endoscopist, and prolonged training is not required to master the technique. Patients should first undergo endoscopy to assess the esophageal lumen before endosonography; although both procedures can be conveniently combined at the same session, this is not essential. It is advisable to have nursing assistance available while performing esophageal EUS as the patients are sedated and prone to aspiration.

The effectiveness of endosonography in diagnosing, staging, and managing esophageal cancer has been well established in a number of publications.[5-7] These have used the Olympus mechanical radial scanner but the high cost of this device has limited its widespread acceptance. Simple, non-optic EUS probes, such as the curved linear array esophageal ultrasound probe used in this study, are safe, easy to use, and effective in the assessment and management of advanced esophageal cancer; if an appropriate ultrasound console is available, they can be inexpensively acquired as add-on probes. However, the resolution obtained is not yet sufficient to recommend its use for staging of early (T2 or less) esophageal cancers.

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