

Abstract 3144

"Hunting a Ghost for 25 Years – Will We Ever Catch OMD?" - No

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Topic: Oligometastatic NSCLC

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### Abstract

Oligometastatic disease (OMD) is no more and no less than what it says on the label. It is cancer with few metastases, no more than can be counted on the fingers of one hand. A few metastases can be locally eradicated with surgery, image guided thermal ablation (IGTA) or with stereotactic ablative radiotherapy (SABR) but beyond five it becomes increasingly impractical to attempt local control. Total eradication is unlikely and systemic treatment makes more sense. So five or fewer identified metastases fit a working definition of OMD as treatable by local interventions.

'Framing' disease according to suitability for treatment has always been part of clinical practice. Diagnostic frames shift over time. A classic example is the emergence of 'ESRD' (end stage renal disease) as a diagnosis. 18thC diagnoses depended on clinical descriptions. 'Dropsy' was illness characterised by water retention; what we call oedema. William Withering observed that some of those sick with dropsy were helped by infusions of foxglove. Later Richard Bright discovered protein in the urine of others. At autopsy he found shrivelled kidneys and dropsy had to be reframed, depending on whether it was the heart or the kidneys that were failing. Aetiology, pathophysiology, and histology sequentially framed the many types of kidney disease through the 1960s but effective treatment only became available with dialysis and transplantation. Long-term survival was possible but was too costly for nearly all individuals and their families. In 1972 US Congress passed Public Law 92-603 which framed a new diagnosis: ESRD. Patients with end stage renal disease were entitled to federal funding. In 1974 ESRD appeared for the first time in PubMed in a paper about public financing. ESRD has been used in titles or abstracts 15,282 times since and runs at over a thousand citations a year.

Hellman and Weichselbaum proposed the term 'oligometastases' in 1995 to describe a clinical state between freedom from metastases and their 'extensive and widespread' presence. (Figure) A search for <oligometas\*> reveals very few publications for about 10 years. Improving resolution of CT, and then PET imaging, allowed the counting of macroscopic metastases by being more confident of the *absence* of further macroscopic metastases. That was a prerequisite to diagnose OMD. Weichselbaum had in mind that "recognition ... of a state of oligometastases is necessary to invite active clinical investigation of new and potentially curative therapeutic strategies". In practical terms it is the therapeutic opportunity that makes OMD a useful working diagnosis, summarised as few enough to 'zap'. In 2015 Joseph Salama surveyed radiation oncologists on their clinical practice and opinions; 99% of 1007 regarded OMD as something for them to treat.

It is the feasibility of treatment which characterises OMD. Many diseases are framed and reframed by whether they are amenable to treatment. A familiar example was the emergence of non small-cell lung cancer (NSCLC) as a diagnostic frame. In the 1970s, adenocarcinoma, squamous cell, and large cell anaplastic cancer had 25-30% five-year survival after lobectomy, but surgery for small-cell cancers nearly always failed. Conversely

chemotherapy for lung cancer, then associated with modest responses, caused small-cell carcinoma to melt away, if only temporarily. It may seem strange to frame a disease by *what it is not*, but that is how NSCLC was framed. Lung cancer was dichotomised on the basis of response to treatments.

We used 'SBE' for subacute bacterial endocarditis and 'CVA' for cerebrovascular accident. In the modern world of heart surgery and antibiotic resistance, SBE is no longer a serviceable diagnostic frame. We must be specific about organisms, underlying lesions, and prostheses. With therapeutic interventions available for stroke we have to distinguish bleeding from embolism. The catch-all term 'CVA' will no longer serve. In time NSCLC will no doubt be unbundled on the basis of tumour markers, genomics, and targeted treatments. But in an era when we talk of precision medicine, it is remarkable that the 99 patients in SABR-COMET had more than five different primary and secondary sites, bundled as OMD.

At Guy's our lung cancer meetings were chaired by a lady radiologist who steered us with incisive clarity. She and I discussed treatment of metastases. She was just back from a trip to the US where she had many similar conversations. "It always ends up with the same question" she told me "Can you charge for it?". So that is the reality. The 1007 radiation oncologists will view the SABR-COMET trial results as the evidence they need. People with ESRD demonstrably survive due to treatment but OMD does no more than identify patients at the tail of the survival distribution, those most likely to live a while longer. Attributing their survival to treatment of a few metastases that can be seen is largely illusory. If sound biological science is the Ghost we seek, we haven't caught it yet.

nscl omd for iaslc abstract.jpg

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