THE SAFETY AND FEASABILITY OF TRANSITIONING FROM TRANSFEMORAL TO TRANSRADIAL ACCESS LEFT VENTRICULAR ENDOMYOCARDIAL BIOPSY.

Authors:

Zaccharie Tyler[1], Oliver P. Guttmann[1,2], Mehul Dhinoja[1], Rodnie Oro[1], Konstantinos Savvatis[1,2], Saidi Mohiddin[1,2], Neha Sekhri[1,2], Luis Lopes[1,2], Vimal Patel[1], Daniel A. Jones[1], Christos V. Bourantas[1], Anthony Mathur[1], Perry M Elliott[1,2], Constantinos O'Mahony [1,2].

Corresponding author:

Dr Constantinos O'Mahony, St Bartholomew's Hospital, London EC1A 7BE, United Kingdom.

Tel: +44-203-456-4801

Fax: +44-207-456-4901

Email: drcostasomahony@gmail.com

Word count: main text 1953, references 485

Affiliations:

1. St Bartholomew's Hospital, West Smithfield, London EC1A 7BE, UK.

2. UCL Centre for Heart Muscle Disease, Institute of Cardiovascular Science, University College London, Gower St, London WC1E 6BT, UK.

ABSTRACT

Introduction: Left ventricular endomyocardial biopsy (LVEMB) is commonly performed via the transfemoral route. Radial access may help reduce vascular access complications but there are few data on the safety and feasibility of transradial LVEMB.

Objective: Describe the safety and feasibility of transitioning from transfemoral to transradial access LVEMB.

Methods: This is a single centre, prospective observational cohort study. Fifty procedures in 49 patients were included, 25 (50%) via the femoral route and 25 (50%) via the radial route.

Results: The cohort had a mean age of 47±13 years and the commonest indication for LVEMB was myocarditis. From June 2015 till September 2016, all procedures were performed via the femoral approach (n=21) and thenceforth there was a gradual transition to the radial approach. More tissue samples were obtained when the procedure was performed via the femoral approach (p=0.003). The minimum sampling target of 3 specimens was not met in 4 (16%) patients via the radial approach and in 1 (4%) patient via the femoral approach. Complications occurred in 3/25 (12%) transradial procedures (2 cardiac perforations and 1 forearm haematoma) and 3/25 (12%) transfemoral LVEMB (1 cardiac perforation, 1 femoral artery pseudoaneurysm and 1 ventricular fibrillation). Cardiac perforations via the transradial approach occurred during the early transition period. There were no deaths.

Conclusions: Transradial LVEMB is feasible, with a similar complication profile as femoral procedures but associated with a smaller number of specimens. Transitioning from transfemoral to transradial procedures may initially be associated with a higher risk of complications and potentially a lower diagnostic yield.

INTRODUCTION

Endomyocardial biopsy is an important diagnostic tool in the workup of patients with non-ischaemic cardiomyopathy. In recent years left ventricular endomyocardial biopsy (LVEMB) has supplanted right ventricular endomyocardial biopsy as the method of choice for obtaining cardiac tissue (1–3). LVEMB is conventionally undertaken via the transfemoral route but the radial artery has become the access route of choice for most coronary interventions and diagnostic procedures due to reduced complication rates, early mobilisation and reduced hospital stay (4,5). Adoption of the transradial route for LVEMB has been slow, partly due to the larger diameter catheters used to accommodate bioptomes, with few available data (6–11). The objective of this study was to describe the safety and feasibility of transitioning from transfemoral to transradial LVEMB.

METHODS

Study design and patient population

This is a single centre observational cohort study. All patients who underwent a LVEMB between June 2015 and October 2019 were considered. During this period LVEMB transitioned from the transfemoral to the transradial route. Procedural data were prospectively collected in a dedicated database (Dendrite Clinical Systems Ltd) in accordance to local protocols. Data analysis was approved by Barts Health NHS Trust Clinical Effectiveness unit as part as part of a local audit (ID: 10646). All authors have read and agree to the manuscript as written.

Overview of procedures

All patients were reviewed by a specialist cardiomyopathy team and referred for LVEMB. Anticoagulants were withheld prior to the procedure which was always undertaken with an INR<1.6 and platelet count >50x10^9/L. Echocardiography was carried out in the catheterisation laboratory immediately prior to the procedure to establish baseline mitral valve function and to detect and quantify pre-existing pericardial effusions. All patients had intra-procedural ECG, invasive arterial/LV

pressure monitoring and oxygen saturations. Intra-venous or intra-arterial heparin was administered. LV-grams (Right Anterior Oblique (RAO) 30-45◦ with an additional Left Anterior Oblique (LAO) 30◦ LV-gram at the discretion of the operator) were taken to guide the biopsy. The procedures were carried by 3 operators [OG, MD, COM] with the aim to obtain a minimum of 3 specimens. In a subgroup of patients, coronary angiography and/or right heart catherization were undertaken at the same setting. Once the sampling was complete, further LV-gram(s) and echocardiography were performed to assess pericardial fluid and mitral regurgitation. Haemostasis was pursued after a satisfactory period of invasive haemodynamic monitoring (minimum of 5 minutes). After 4 hours of post-procedural observation (cardiac monitoring, saturations, and non-invasive BP) elective outpatients without complications were discharged.

LVEMB via the radial approach: technical aspects

A 5.5F (length: 104cm) Cordis (Cardinal Health, Milpitas, CA) bioptome was used for all procedures. A 6F multipurpose (MP) guide (length 100cm) was shortened by 10cm at the proximal end and attached to a shortened 5Fr femoral sheath to allow introduction of the bioptome and haemodynamic monitoring via the side port. Shortening the multipurpose catheter is essential to allow the bioptome to have enough reach in the LV. The technical steps are shown in figure 1. After radial access was gained with a 6F radial sheath, 2.5mg of verapamil were given by the radial sheath to prevent spasm. A 5Fr pigtail catheter was then introduced into the lumen of the 6F MP guide and advanced over a 0.035" guidewire under fluoroscopic guidance to the ascending aorta. The aortic valve was crossed with the pigtail catheter and the aid of the 0.035" wire. At this point LV grams are obtained as roadmaps. The tip of the MP guide catheter was then positioned in the mid cavity of the LV over the pigtail catheter, which was then removed. Position of the MP guide was confirmed in orthogonal planes (right anterior oblique 30-45° and left anterior oblique 30-45°). To confirm that the MP catheter was not abutting the LV wall, approximately 5 ml of contrast were injected under fluoroscopy. The Cordis bioptome was then advanced through the MP guide catheter into the LV

cavity. Samples were obtained with fluoroscopic guidance. Repetitive bleed-back and manual flushing were undertaken to avoid air embolization during sample extraction and bioptome reinsertion. Following completion of the procedure the radial sheath was removed and a haemostatic band was positioned.

LVEMB via the femoral approach

A transfemoral biopsy was performed utilising the same equipment or alternatively using a 7F 90cm sheath.

Procedural complications

Patient records were reviewed and the following procedural complications were recorded: pericardial effusion, pericardial drain or window for cardiac tamponade, mitral valve surgery, peri-procedural stroke, ventricular arrhythmias, bradyarrhythmia requiring pacing, refractory radial artery spasm, access site bleeding, haematomas, arteriovenous fistulae, false aneurysms, limb ischaemia, and need for blood transfusion.

Statistical methods

Variables are expressed as mean ± standard deviation (SD), median (25^{th} to 75^{th} percentiles) or counts and percentages as appropriate. Differences between means were compared using the Student t-test and the Mann-Whitney U test for normally-distributed and non-normally-distributed continuous data, respectively. Categorical data were compared using the Pearson Chi-squared test. A two-sided $p<0.05$ was considered statistically significant. This study is not powered to detect differences. All statistical analyses were carried out using STATA (version 11).

RESULTS

During the study period a total of 53 procedures were undertaken in 52 patients. Three procedures were excluded due to missing data. A total of 50 LVEMB in 49 patients were included in the analysis. All patients were adults (age range: 16.4 to 69.1 years), and most were male undergoing the

procedure electively for investigation of myocarditis. The right radial artery was utilised in 25 (50%) procedures; the femoral approach was used for the remaining 25 (50%) biopsies. The baseline clinical characteristics are shown in table 1.

From June 2015 till September 2016, all procedures were performed via the femoral approach (n=21) and thenceforth there was a gradual transition to the radial approach as shown in figure 2. There was no significant difference in sex (p=0.24) or urgency (p=0.14) between the two approaches.

Complications

Complications occurred in 6 (12%) patients: 3 via the right radial artery (RRA) and 3 via the femoral approach. There were no deaths. The complications are listed in table 1 and described in detail below.

1. Vascular complications

Two patients suffered vascular complications. A 44-year-old male had a traumatic radial sheath insertion complicated by a forearm haematoma treated with manual pressure; the LVEMB was undertaken without complication via the right femoral artery 2 months later. A 46-year-old female with left ventricular hypertrophy (LVH), investigated for an inborn error of metabolism, developed bleeding from the right femoral artery during recovery and developed a haematoma with a 0.4cm pseudo aneurysm which resolved with conservative treatment.

2. Arrhythmic complications

A 47-year-old man with unexplained LVH developed ventricular fibrillation following contrast injection via the MP catheter after the 4th biopsy was taken was taken via the right femoral artery. Defibrillation was successful and was discharged uneventfully.

3. Cardiac perforations

Three patients had cardiac perforation with a prevalence of 6% (95% CI 0.0 to 13%). A 32-year-old man with unexplained LVH developed cardiac tamponade after 3 biopsies were taken via the right femoral artery. Pericardiocentesis was performed without the need for surgery and he had an uneventful recovery. A 71-year-old lady with unexplained LVH developed a pericardial effusion with tamponade after taking 1 sample via the RRA (this was the fourth consecutive radial LVEMB). Pericardiocentesis was performed, blood was transfused, and the bleeding settled without the need for cardiac surgery. A 29-year-old female with fulminant myocarditis developed a small pericardial effusion after withdrawing the bioptome during the first sampling attempt via the RRA (this was the eighth consecutive radial LVEMB). Pericardiocentesis was not required but the procedure was abandoned, and samples were not obtained. Beyond the eighth consecutive transradial LVEMB, no other cardiac perforations occurred.

Number of specimens obtained

The median number of pieces in the whole cohort was 5 (3 to 5). The median number of specimens with the transfemoral approach was 5 (4 to 5) and with the transradial approach was 4 (3 to 5). More tissue samples were obtained when the procedure was performed via the femoral approach (p=0.003) as shown in figure 3A. This difference persisted when cases with complications were excluded from this analysis (p=0.007). Three or more specimens were obtained in 45 procedures (90%). The minimum sampling target of 3 specimens was not met in 4 (16%) LVEMB via the transradial approach and in 1 (4%) patient via the transfemoral approach (figure 3B). With the exception of two procedures (29-year-old with pericardial effusion and 44-year-old with forearm haematoma as described above), LVEMB specimens of sufficient quality for histological examination were obtained.

DISCUSSION

This single centre study shows that during the early phase of radial access adoption, LVEMB carries a similar procedural risk to femoral access procedures but less specimens were obtained. These

findings are in the context of a transition from femoral to radial access LVEMB and will inform other practitioners who are considering adoption of the radial approach.

The safety of radial over femoral access, convincingly demonstrated in percutaneous coronary intervention (12–14), has catalysed its uptake in LVEMB in some centres. To date, there are limited data on radial access LVEMB with only a small number of published studies. To our knowledge Bagur et al (6) published the first case in 2014 and soon after a series of 37 patients reported no vascular access site complications but one patient developed intra-procedural ventricular fibrillation and another developed a cerebrovascular accident (8). A recently published international, multicentre study (incorporating Schaufele et al 2015 and Choudhury et al 2018 (7,11)) with 130 transradial procedures and 134 transfemoral procedures demonstrated the safety of the radial approach which was associated with fewer vascular complications (15). The current study lends further weight to the evidence that LVEMB can be safely performed via the radial artery, without clinically significant vascular complications.

Even though there were no deaths in our cohort, the rate of complications in the transradial access group was higher compared to other previously described studies (7,8,11,15). This may be explained by the learning curve associated with the adoption of the radial approach during the study period, differences in equipment and cohort characteristics. Most other studies used sheathless 7.5F MP1 guiding catheters which may allow easier, frictionless manipulation of the bioptome compared to the modified 6F MP1 used in our institution. The different bioptomes used in each centre, each with different stiffness and cutting characteristics, may also account to some extend for the complication rates. Finally, our cohort is younger (mean age in 5th decade of life) in comparison to the other studies (mean age 6th decade of life) which is likely to reflect the underlying disease process and perhaps predisposition for certain complications.

The smaller number of specimens via the radial approach may be explained by the limited initial experience of radial access LVEMB. The occurrence of 2 cardiac perforations at the very beginning of

the transition to radial access is likely to have contributed to a more conservative sampling strategy by the operators. Like with any procedure, it is expected that the prevalence of complications will decline with increased experience but data to demonstrate this are not currently available.

The findings of this report are limited by the observational nature of the study, which is not powered to categorically compare the features of the two access routes.

CONCLUSIONS

Transradial LVEMB is feasible and relatively safe using modified guiding catheters but associated with a smaller number of specimens. During the transition from transfemoral to transradial access, LVEMB may initially be associated with a higher risk of complications and potentially a lower number of specimens.

FUNDING SOURCES

This work was undertaken at St Bartholomew's Hospital who received a proportion of funding from the United Kingdom Department of Health's National Institute for Health Research Biomedical Research Centres funding scheme.

CONFLICTS OF INTEREST

None declared.

REFERENCES

1. Yilmaz A, Kindermann I, Kindermann M, Mahfoud F, Ukena C, Athanasiadis A, et al. Comparative evaluation of left and right ventricular endomyocardial biopsy: Differences in complication rate and diagnostic performance. Circulation. 2010;122(9):900–9.

2. Frustaci A, Pieroni M, Chimenti C. The role of endomyocardial biopsy in the diagnosis of cardiomyopathies. Ital Hear J. 2002;3(6):348–53.

3. Chimenti C, Frustaci A. Contribution and risks of left ventricular endomyocardial biopsy in patients with cardiomyopathies: A retrospective study over a 28-year period. Circulation. 2013;128(14):1531–41.

4. Mitchell MD, Hong JA, Lee BY, Umscheid CA, Bartsch SM, Don CW. Systematic review and cost-benefit analysis of radial artery access for coronary angiography and intervention. Circ Cardiovasc Qual Outcomes. 2012;5(4):454–62.

5. Jolly SS, Yusuf S, Cairns J. Erratum: Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): A randomised, parallel group, multicentre trial (The Lancet (2011) 377 1409-1420). Lancet. 2011;378(9785):30.

6. Bagur R, Bertrand OF, Beliveau P, Gaudreault V, Potvin JM, Fillion N, et al. Feasibility of using a sheathless guiding catheter for left ventricular endomyocardial biopsy performed by transradial approach. J Invasive Cardiol. 2014;26(12):E161–3.

7. Schäufele TG, Spittler R, Karagianni A, Ong P, Klingel K, Kandolf R, et al. Transradial left ventricular endomyocardial biopsy: assessment of safety and efficacy. Clin Res Cardiol. 2015;104(9):773–81.

8. Schulz E, Jabs A, Gori T, Hink U, Sotiriou E, Tschöpe C, et al. Feasibility and safety of left ventricular endomyocardial biopsy via transradial access: Technique and initial experience. Catheter Cardiovasc Interv. 2015;86(4):761–5.

9. Bagur R, Gilchrist IC. Transradial approach to take a little piece of heart. Catheter Cardiovasc Interv. 2015;86(4):766–7.

10. Kherad B, Köhncke C, Spillmann F, Post H, Noutsias M, Pieske B, et al. Postprocedural radial artery occlusion rate using a sheathless guiding catheter for left ventricular endomyocardial biopsy performed by transradial approach. BMC Cardiovasc Disord [Internet]. 2016;16(1):1–7. Available from: http://dx.doi.org/10.1186/s12872-016-0432-y

11. Choudhury T, Schäufele TG, Lavi S, Makino K, Nobre Menezes M, Solomonica A, et al. Transradial Approach for Left Ventricular Endomyocardial Biopsy. Can J Cardiol. 2018;34(10):1283–8.

12. Baklanov D V., Kaltenbach LA, Marso SP, Subherwal SS, Feldman DN, Garratt KN, et al. The prevalence and outcomes of transradial percutaneous coronary intervention for st-segment elevation myocardial infarction: Analysis from the national cardiovascular data registry (2007 to 2011). J Am Coll Cardiol. 2013;61(4):420–6.

13. Joyal D, Bertrand O, Rinfret S, Shimony A, Eisenberg M. Meta-analysis of ten trials on the effectiveness of the radial versus the femoral approach in primary percutaneous coronary intervention. Am J Cardiol. 2012;109(6):813–8.

14. Brener MI, Bush A, Miller JM, Hasan RK. Influence of radial versus femoral access site on coronary angiography and intervention outcomes: A systematic review and meta-analysis. Catheter Cardiovasc Interv. 2017;90(7):1093–104.

15. Choudhury T, Lurz P, Schäufele TG, Menezes MN, Lavi S, Tzemos N, et al. Radial versus femoral approach for left ventricular endomyocardial biopsy. EuroIntervention. 2019;15(8):678–84.

Table 1: Clinical characteristics

	All procedures n=50	**Radial access procedures n=25**	**Femoral access procedures n=25**
Age, years	47±13	48±15	46±11
Male	32 (64%)	18 (72%)	14 (56%)
LVEF (%)	48±14	48±13	48±15
Platelet count (x10^9/l)	261±77	258±92	263±60
Atrial fibrillation	9 (18%)	3 (12%)	6 (24%)
eGFR (ml/min/1.73m^2)	79±24	69±17	90±25
Indication:			
• Myocarditis	34 (68%)	20 (80%)	14 (56%)
• Sarcoid	9 (18%)	3 (12%)	6 (24%)
• Metabolic disease	5 (10%)	0	5 (20%)
• Amyloid	2 (4%)	2 (8%)	0
Elective	33 (66%)	14 (56%)	19 (76%)
Number of biopsy samples	5 (3 to 5)	4 (3 to 5)	5 (4 to 5)
Pericardial effusion/perforation (total):	3 (6%)	2 (8%)	1 (4%)
• Pericardial drain	2 (4%)	1 (4%)	1 (4%)
• Conservative management	1 (2%)	1 (4%)	0
Mitral valve surgery	0	0	0
Bradyarrhythmia requiring pacemaker	0	0	0
Ventricular arrhythmia	1 (2%)	0	1 (4%)
Peri-procedural stroke	0	0	0
Vascular access site complication	2 (4%)	1 (4%)	1 (4%)
Limb ischaemia	0	0	0

Variables are expressed as mean ± standard deviation (SD), median (25^{th} to 75^{th} centile) or counts and percentages as appropriate.

FIGURE LEGENDS:

Figure 1:

Equipment for endomyocardial biopsy. Panel A: 5.5F (length: 104cm) Cordis (Cardinal Health, Milpitas, CA) bioptome is used for all procedures. Panels B-F: A 6F multipurpose (MP) guide (length 100cm) was shortened by 10cm at the proximal end and attached to a shortened 5Fr femoral sheath to allow introduction of the bioptome and haemodynamic monitoring via the side port. Panels G-H: A 5Fr pigtail catheter is then introduced into the 6F MP guide and is advanced over a 0.035" guidewire under fluoroscopic guidance up to the ascending aorta. The aortic valve was crossed with the pigtail catheter with the aid of the 0.035" wire. Panels I-J: The tip of the MP guide catheter was then positioned in the mid cavity of the LV over the pigtail catheter, which was then removed. The Cordis bioptome is then advanced through the MP guide catheter into the LV cavity.

Figure 2:

The proportion for radial and femoral access LVEMB arranged by chronological order (the first and last LVEMB labelled as 1 and 50 respectively). With time, there is a gradual transition from the femoral to the radial approach.

Figure 3A:

The box plots show the variation in the number of pieces obtained by each approach. The red dot within the box represents the median; the upper and lower edges of each box represents the 25th and 75th percentiles (Q1 and Q3); the ends of the whiskers are the upper and lower adjacent values within Q3+1.5*(Q3-Q1) and Q1-1.5*(Q3-Q1); outliers are shown as blue dots.

Figure 3B:

The vertical reference lie represents the minimum sampling requirement. The minimum sampling target of 3 specimens was not met in 4 (16%) patients via the radial approach and in 1 (4%) patient via the femoral approach.

Figure 1A

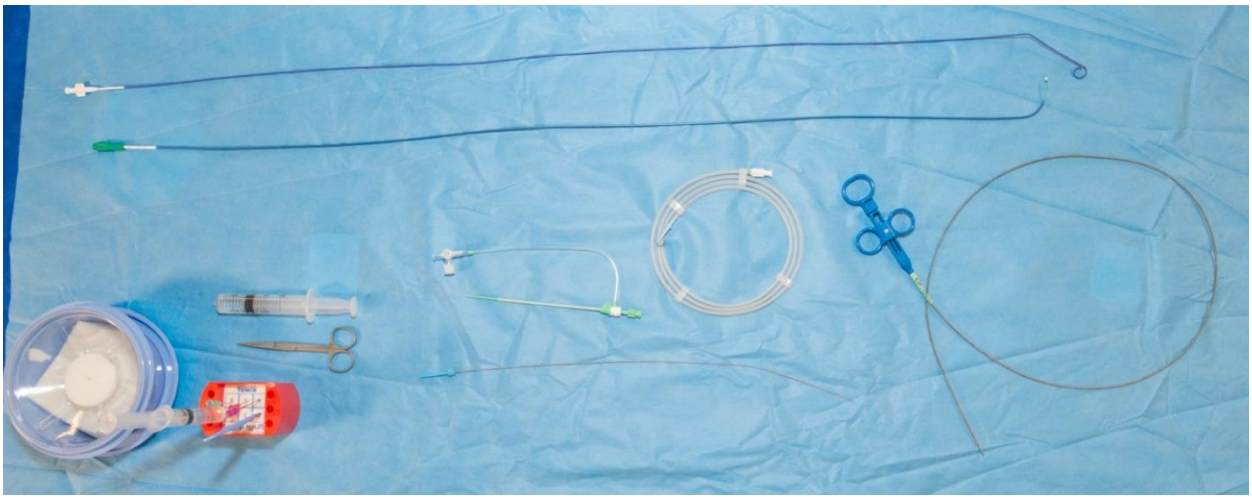

Figure 1B

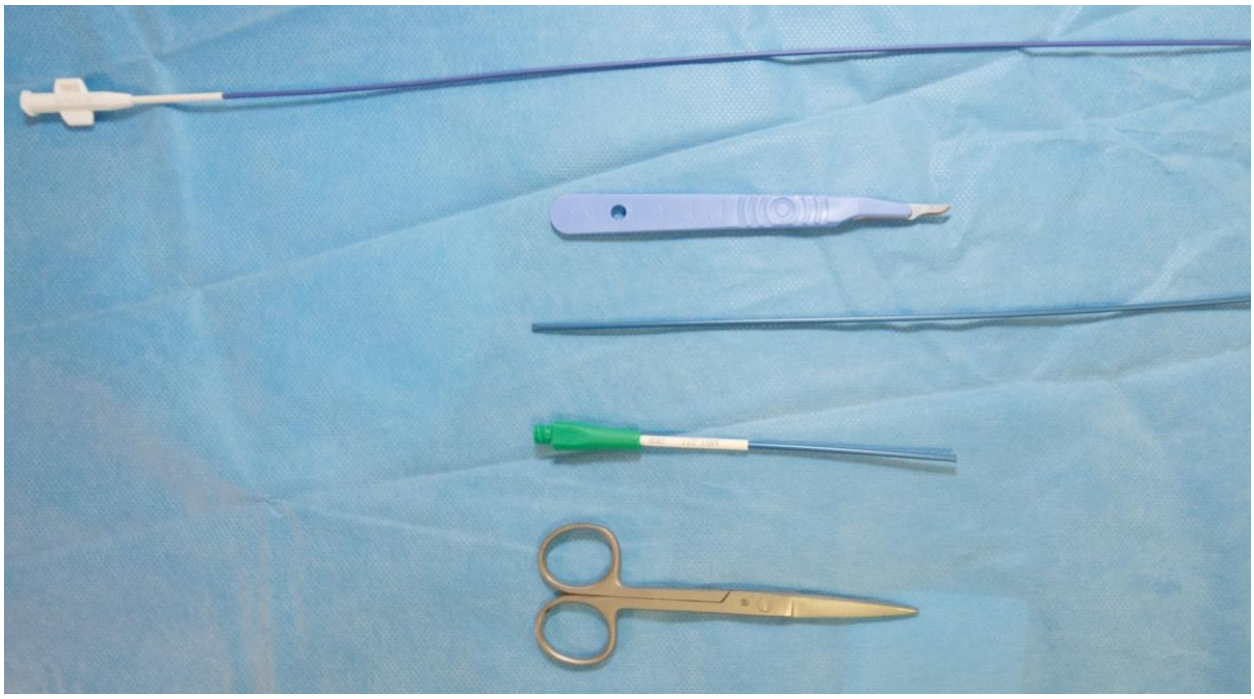

Figure 1C

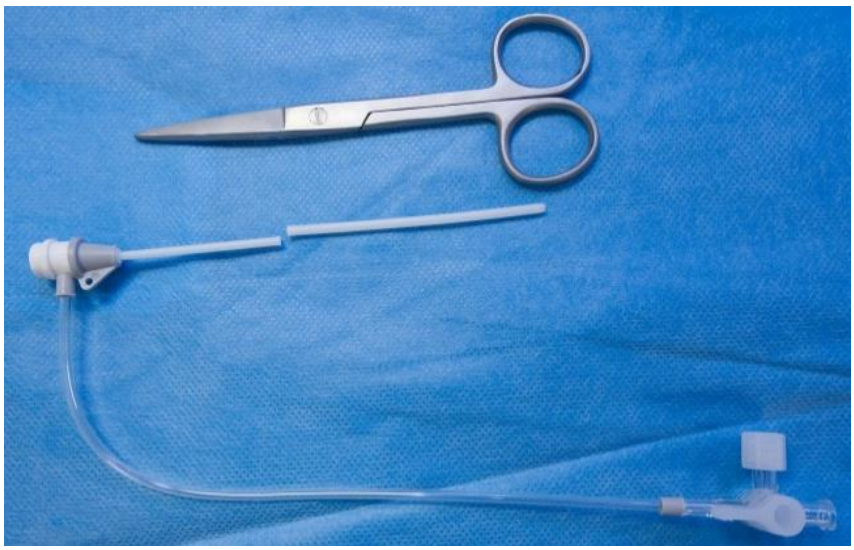

Figure 1D

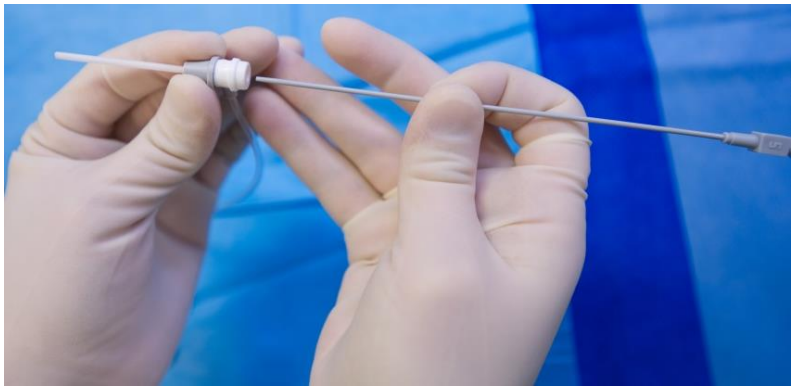

Figure 1E

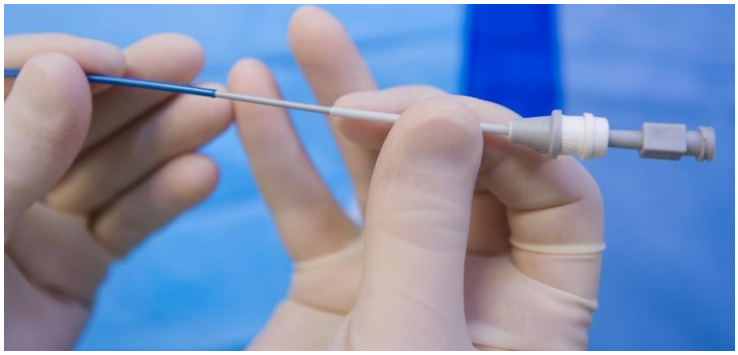

Figure 1F

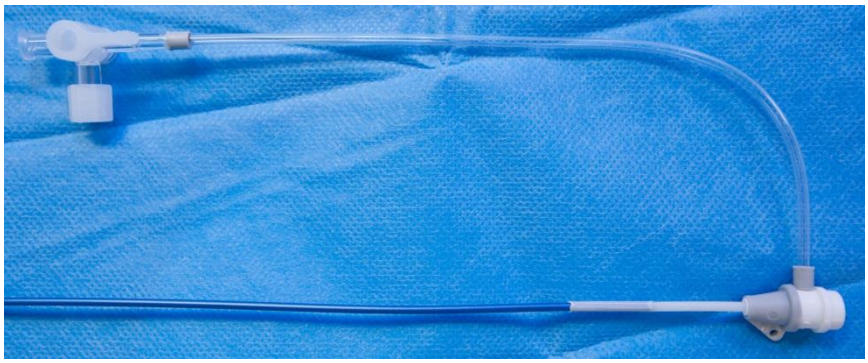

Figure 1G

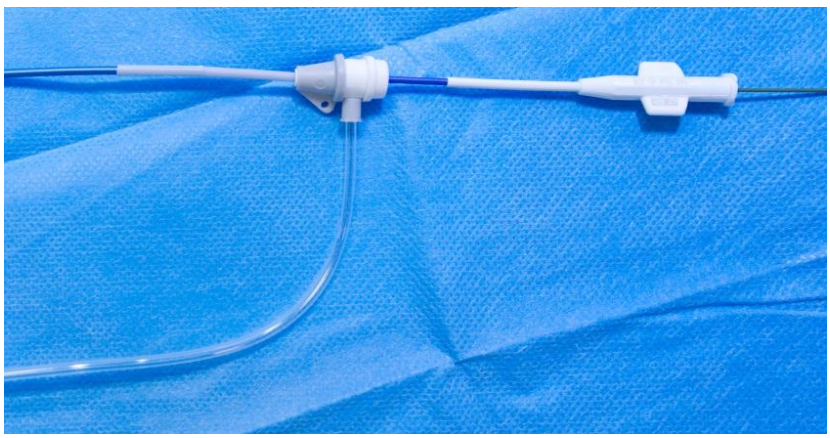

Figure 1H

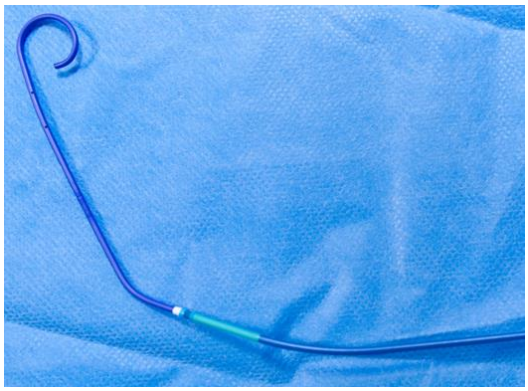

Figure 1I

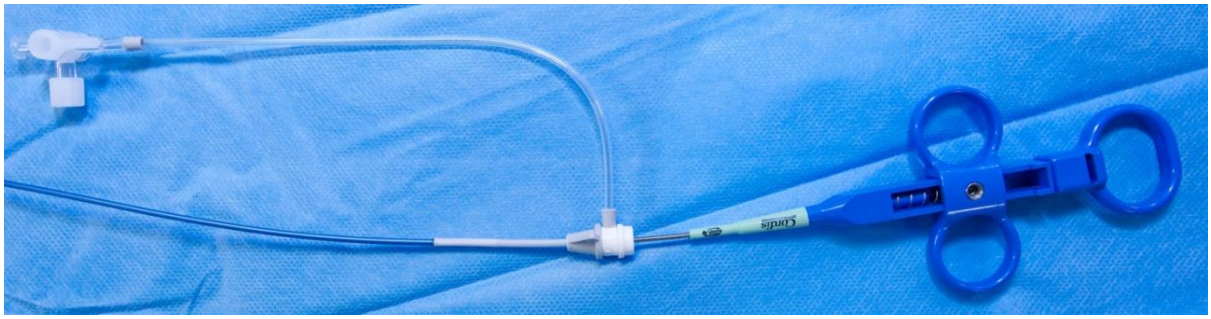

Figure 1J

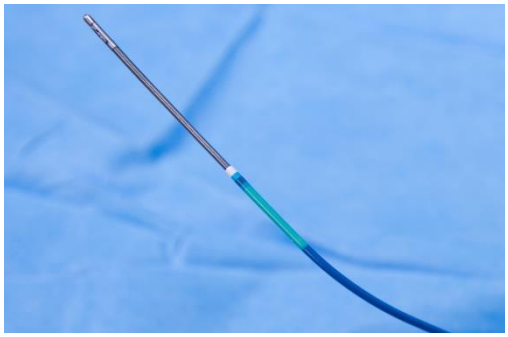

Figure 2: The transition from the femoral to the radial approach.

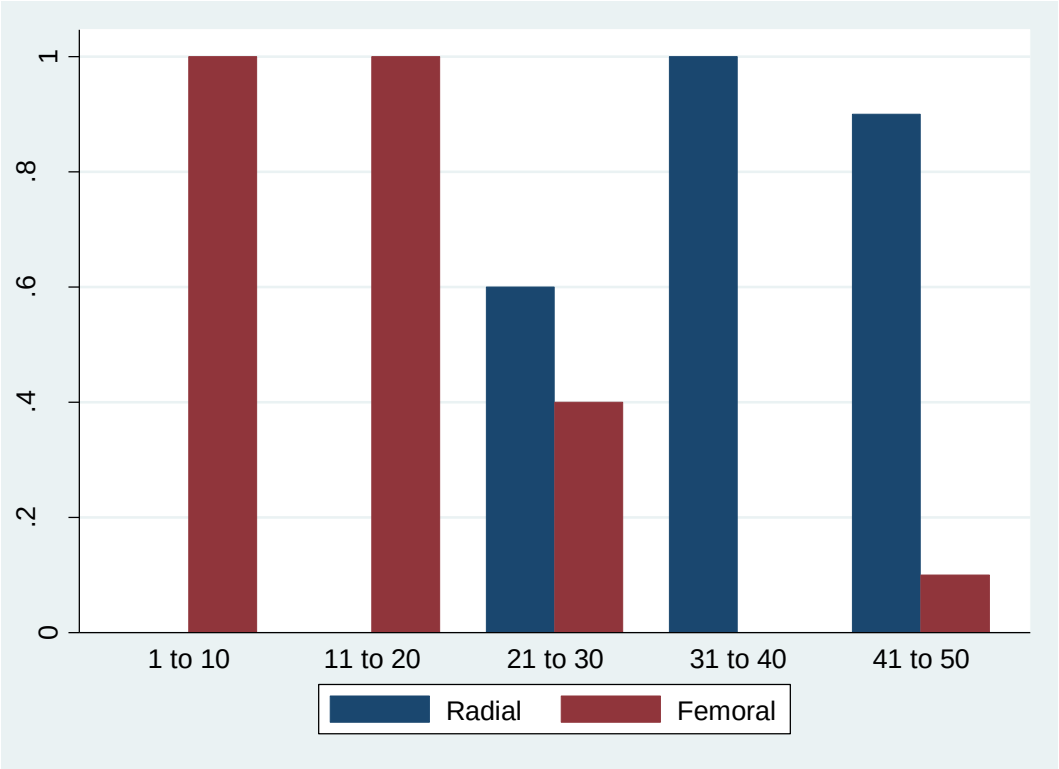

Figure 3A: The number of tissue specimens with each approach.

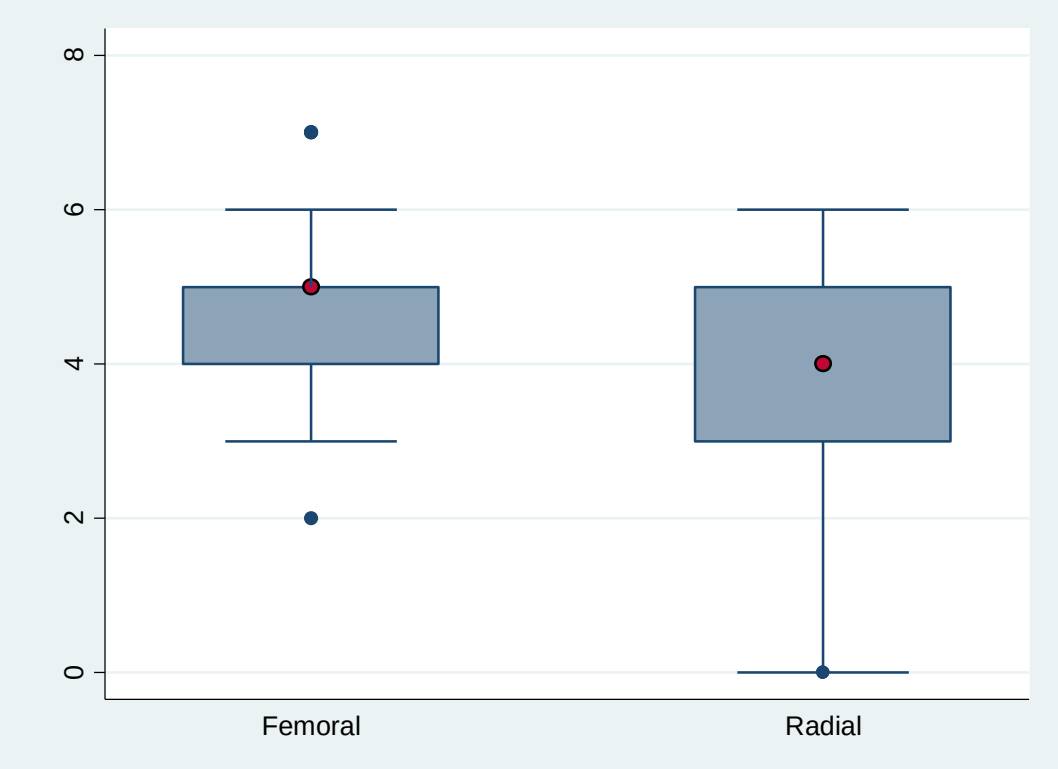

Figure 3B: The variability in the samples taken for each access route