Autologous microsurgical breast reconstruction and coronary artery bypass grafting – An anatomical study and clinical implications

Warren M Rozen[1], MBBS BMedSc PGDipSurgAnat PhD *

Xuan Ye[1], MBBS (Hons)*

Pedro L Guio-Aguilar[1], BSc (Biotech) MD

Alberto Alonso-Burgos, MD

John Goldblatt[2], MBBS FRACS

Mark W Ashton[1], MBBS MD FRACS

Iain S Whitaker[1,3], BA (Hons) MA Cantab MBBChir MRCS PhD FRCS Plast.

*** Denotes equal first author**

1 Jack Brockhoff Reconstructive Plastic Surgery Research Unit, Department of Anatomy and Cell Biology, The University of Melbourne

2 Department of Cardiothoracic Surgery, Royal Melbourne Hospital.

3 Swansea University College of Medicine, Singleton Park, SA2 8PP, Swansea, Wales , UK

Correspondence and reprints: Dr Warren Matthew Rozen. Jack Brockhoff Reconstructive Plastic Surgery Research Unit, Department of Anatomy and Cell Biology, The University of Melbourne, Grattan St, Parkville, Victoria, 3050, Australia.

Email: warrenrozen@hotmail.com   Phone: +613 9347-5939

Running Title: The IMA in breast reconstruction & CABG

Mini-Abstract

The optimal autologous reconstructive technique for breast reconstruction and coronary artery bypass grafting (CABG) are potentially mutually exclusive as they both require utilisation of the internal mammary arteries (IMAs) as the preferred arterial conduit. Through an anatomical study and literature review, we propose four methods for overcoming this predicament, and discuss long term implications.

Abbreviations:

BIMA	Bilateral internal mammary artery
CABG	Coronary artery bypass graft
CTA	Computer tomography angiogram
DIEP	Deep inferior epigastric artery perforator
DSEA	Deep superior epigastric artery
ICS	Intercostal space
IMA	Internal mammary artery
IMAP	Internal mammary artery perforator
IMV	Internal mammary vein
LAD	Left anterior descending artery
LIMA	Left internal mammary artery
OECD	Organisation for Economic Co-operation and Development
MRI	Magnetic resonance imaging
RIMA	Right internal mammary artery

Structured Abstract

OBJECTIVE: To identify possible avenues of sparing the internal mammary artery (IMA) for coronary artery bypass grafting (CABG) in women undergoing autologous breast reconstruction with deep inferior epigastric artery perforator (DIEP) flaps.

BACKGROUND: Optimal autologous reconstruction of the breast and coronary artery bypass grafting (CABG) are often mutually exclusive as they both require utilisation of the IMA as the preferred arterial conduit. Given the prevalence of both breast cancer and coronary artery disease, this is an important issue for women's health as women with DIEP flap reconstructions and women at increased risk of developing coronary artery disease are potentially restricted from receiving this reconstructive option should the other condition arise.

METHODS: The largest clinical and cadaveric anatomical study (n=315) to date was performed, investigating four solutions to this predicament by correlating the precise requirements of breast reconstruction and CABG against the anatomical features of the in-situ IMAs. This information was supplemented by a thorough literature review.

RESULTS: Minimum lengths of the left and right IMA needed for grafting to the left-anterior descending artery are 160·08mm and 177·80mm respectively. Based on anatomical findings, the suitable options for anastomosis to each intercostals space are offered. In addition, 87-91% of patients have IMA perforator vessels to which DIEP flaps can be anastomosed in the 1st and 2nd intercostal spaces.

CONCLUSION: We outline five methods of preserving the IMA for future CABG: 1) lowering the level of DIEP flaps to the 4th and 5th intercostals spaces; 2) using the DIEP pedicle as an intermediary for CABG; 3) using IMA perforators to spare the IMA proper; 4) using and end-to-side anastomosis between the DIEP pedicle and IMA; and 5) anastomosis of DIEP flaps using retrograde flow from the distal IMA. With careful patient selection, we hypothesize using the IMA for autologous breast reconstruction need not be an absolute contraindication for future CABG.

Introduction

Breast cancer and coronary artery disease are two leading causes of morbidity and mortality in women. Fortunately, they are amenable to surgical intervention in the forms of mastectomy with subsequent breast reconstruction and coronary artery bypass grafting (CABG). However, the optimal technique for autologous breast reconstruction [1-8], the deep inferior epigastric artery perforator (DIEP) flap using the internal mammary artery as the recipient vessel, and the IMA based CABG are mutually exclusive as they both require utilisation of the IMAs as an arterial conduit [9-15]. In theory, this may preclude women with pre-existing DIEP reconstructions from receiving CABGs (with proven survival benefit), and women at increased risk of developing coronary artery disease from receiving what many surgeons consider to be the optimal autologous breast reconstruction post-mastectomy. In the light of the prevalence of both conditions, we believe investigating potential strategies to overcome this problem is of importance to women's health.

Background

Breast Cancer

Breast cancer is the leading cause of cancer in women [16-19]. Each year, over 690,000 women are diagnosed with breast cancers in high-income countries at a rate of 83·2 new breast cancers per 100,000 population [17]. Of the women who elect for treatment, 44·3% receive mastectomy [20]. In 2010, 61·5 mastectomies were performed per 100,000 people in countries of the Organisation for Economic Co-operation and Development (**OECD**), making it one of the most common surgical procedures in women of the developed world (Table 1) [18]. Breast reconstructions are often necessary to remodel the defect and restore quality of life. In 2009, over 86,000 breast reconstructions were performed in the United States alone, a statistic which has exhibited a distinct upwards trend [21]. Currently, autologous tissue is the reconstructive option in suitable patients, is with autologous tissue. The DIEP flap is widely believed to yield excellent aesthetic outcomes with minimal donor site morbidity. Although the American Society of plastic surgeons (ASPS) procedural statistics in 2010 show that implant based breast reconstruction remains the most practiced form of breast reconstruction in the US (77%), with DIEP flap reconstruction being the 3rd most frequent reconstruction (5.5 %) behind latissimus flap reconstructions (6.8%) [21], this is not because implant reconstructions produce the best results, it is due to financial pressures imposed by health insurance providers as microsurgical procedures are time and cost intensive [22]. There is some evidence that this may change in the future as experienced microsurgeons argue that the relative increase in cost is worthwhile when considering superior outcomes [23] (See Figure 1). DIEP flaps, in many surgeons hands are anastomosed to the IMA, often at the 2nd or 3rd intercostals space (ICS), leaving insufficient length for subsequent CABG. This is a particular concern in the setting of bilateral mastectomies as both IMAs are used in the reconstruction. Bilateral procedures currently constitute around 10% of breast cancer operations and are becoming increasingly frequent with the greater use of BRCA gene testing and breast MRI [24-29]. Numerous studies have reported an increasing trend towards IMA based breast reconstructions over the past 10-15 years (See Table 2)[13, 14, 30-33].

Coronary Artery Disease

Heart disease is the biggest cause of mortality in women worldwide. According to the World Health Organisation, 746,208 women died from ischemic events in 2008 in high-income countries and this figure is projected to increase to over 936,000 women by 2030 [16].

The standard interventions for myocardial revascularisation are the CABG and percutaneous coronary intervention. Despite the evolution of drug-eluting stents, studies show that CABG is still preferred in the management of three-vessel disease and left-anterior descending (LAD) as it is associated with lower rates of mortality, myocardial infarction and repeat revascularisation [34]. In 2010, 64·2 CABGs were performed per 100,000 people in OECD countries, one in three of which were in women [18, 35] (Table 1).

Currently, the IMAs are the gold standard CABG conduits in terms of graft patency and patient survival [36-38] (See Table 3). Unlike other arterial conduits, the IMAs appear to be immune to atherosclerosis, vasospasm and endothelial injury [38-40]. This is hypothesized to be due to the IMA's demonstrably higher rates of apoptosis, superoxide dehydrogenase activity and nitric oxide production, which allow it to actively dilate and remodel favourably in response to increases in blood flow [39, 41-43]. Overall, the left IMA (LIMA) has a patency rate of 85-92% at 15 years when grafted to the LAD [38, 44, 45] compared to around 53% for saphenous vein grafts [38, 46]. The right IMA (RIMA) demonstrates identical patency rates to the LIMA when grafted to the LAD although this appears diminishes when grafted to a non-left sided vessel [38]. Recent reports however suggest that the observed inferiority of the RIMA compared to the LIMA is likely to be due to technical factors rather than the biology of the RIMA itself [47].

At present, over 90% of CABGs performed in the United States utilise at least one IMA, most commonly LIMA-LAD [37, 47, 48]. However, there is emerging evidence that the use of two IMAs in bilateral grafting (BIMA) may be superior to and supersede single IMA grafting as the gold standard procedure [38, 41, 49-58]. If this is the case, then there is an even greater imperative to preserve both IMAs. Definitive results from these trials however will not be available for several years [38, 41, 54]. Preserving the IMAs for future CABG is especially important to breast cancer patients as they are at an increased risk for coronary artery disease [59-61]. In fact, coronary heart disease is the main cause of non-cancer related mortality in breast cancer patients treated with adjuvant radiotherapy. When followed up over the longer term, breast cancer patients receiving radiation, especially to the left side, are 1.0 to 2.2 times more likely to suffer a fatal cardiovascular event [10, 59-62]. This statistic is particularly worrisome as according to the TEAM trial, 38.8% mastectomy patients receive adjuvant radiotherapy worldwide [20]. Unfortunately, the exact magnitude of this dilemma remains elusive as there are no reliable means of estimating the precise number of women affected. On the conservative side, one retrospective study only reported an incidence of 0.8% (n=120:1) for the two conditions occurring in the same patient [9]. In contrast, others have suggested that the number needed to treat to save one IMA for CABG is 61:1 and that the average surgeon can be expected to preserve 12 IMAs during their career [10, 13]. Yet another author reported 81 cases of perioperative myocardial infarctions following breast reconstructions during a 4 year period [63]. Ultimately, these estimates are highly variable and possibly understate the true extent of this predicament as the peak incidences of the two diseases occur up to two decades apart and are thus not captured by existing studies (Figure 2). Furthermore, selection biases exist in single operator audits and retrospective studies may not account for the women who choose not to receive one procedure over concerns of the other.

Since the introduction of DIEP flaps, more knowledge has come to light on its long term survival with regards to its pedicle. A number of animal studies and case reports suggest that DIEP flaps can survive after separation from the IMA pedicle 7-9 days postoperatively [15, 64-68] if there is a cutaneous inset. Therefore, if the IMAs anastomosed to the DIEP pedicles are long enough to reach the coronary arteries, they can theoretically be disconnected from the DIEP flap and manoeuvred back into the thoracic cavity to be reused in CABG as needed. To test the feasibility of this theory, we conducted an anatomical study comparing the lengths of the IMAs at every ICS against empirical measurements of IMA length required for grafting to the LAD as reported in the literature. We hypothesise that knowledge of the IMA length at any given level of dissection may allow us to modify the way in which DIEPs are performed in order to preserve a sufficient length of IMA to be reused for future CABG. As a secondary objective, we summarise in the discussion a review of alternative techniques for

DIEP reconstruction. From this, we explore a range of other approaches to spare the IMA to provide a comprehensive review of possible solutions to the current dilemma.

Method

Anatomical Study

A combined cadaveric and clinical anatomical study of 315 hemi-thoracic walls was undertaken following ethics committee approval. Specimens and patients were females of mixed body habitus with mean ages of 82 years (60-98 years) for the cadaveric study and 52 years (30-75 years) for the clinical. The cadaveric study comprised of 75 cadaveric hemi-thoracic walls from 39 cadavers (72 bilateral and 3 unilateral). In each case, plain x-ray angiography of the IMA was undertaken via a well-established technique of direct catheterization and injection with a radio-opaque lead oxide injectant [69] (Figure 3) .

In the clinical study, preoperative imaging was performed in 120 consenting patients prior to undergoing autologous breast reconstruction. Of these, 42 patients underwent computed-tomographic angiography (**CTA**) and 78 patients colour duplex ultrasound (Figure 4). Arterial phase CTA scans were undertaken with intravenous contrast in all cases and comprised of non-ionic iodinated contrast media: Ultravist 370 (Schering, Berlin, Germany) or Omnipaque 350 (Amersham Health, Princeton, USA). Intravenous access was obtained through an antecubital vein with an 18-gauge cannula and injections were performed with a biphasic power injection pump at a flow rate of 4-6 mL/s. Image reformatting was achieved with either Siemens Syngo InSpace (Siemens, InSpace2004A_PRE_19) or Osirix (OsiriX Medical Imaging Software, GPL Licensing Open Source Initiative). For duplex ultrasound, a flow value was assigned to the pulsatile arterial flow in order to accurately identify the IMA.

The key anatomical features measured were the IMA length and diameter at each ICS. The origin of the IMA was measured from the inferior aspect of the clavicle for consistency. The first ICS was defined as the distance between the inferior aspect of the clavicle to the superior aspect of the second rib. Each subsequent ICS was defined as the space between the superior aspects of adjacent ribs (Figure 3). The length of each IMA was measured to its bifurcation into its terminal branches, the deep superior epigastric artery (**DSEA**) and the musculo-phrenic artery. In addition, the presence and diameter of IMA perforators (**IMAP**) were recorded at each ICS.

In the cadaveric study, lengths were measured using a vernier caliper and vessel diameters were measured with a 0·1 mm scaled glass slide and a 10X stereo microscope (Leica® M80 10X/23B). In the clinical study, both length and vessel diameters were measured with the aforementioned software on thin slices with contrast-filled vessels used to highlight internal vessel diameters.

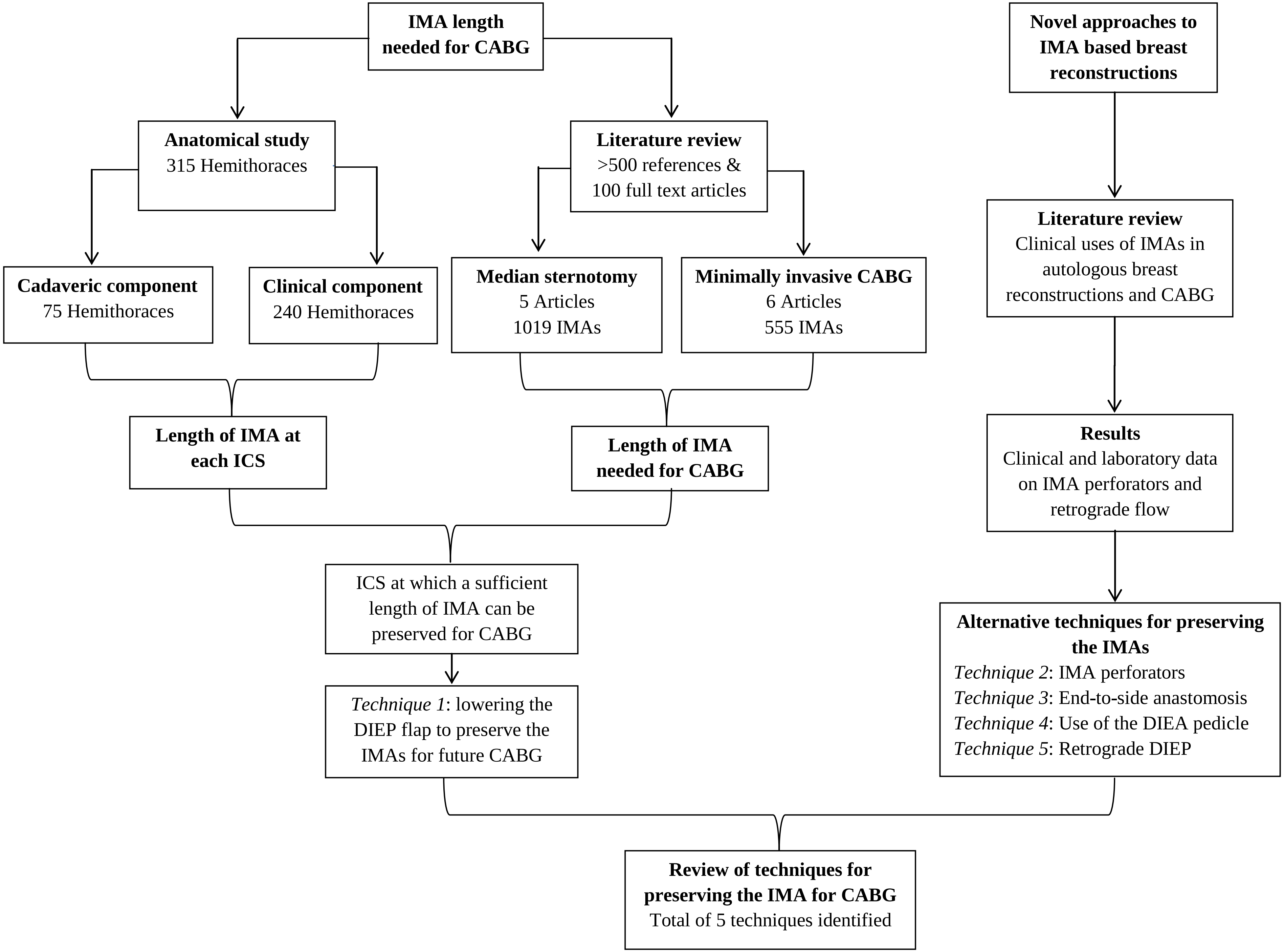
Literature Review

The length of IMA needed for CABG was determined via searches of Medline, Pubmed, and references from relevant articles using the following terms:

- 'Coronary artery bypass grafting/CABG'
- 'internal mammary/thoracic artery';
- 'IMA/LIMA/RIMA';
- 'ITA/LITA/RITA';
- 'length/cm/mm/pedicle';
- 'needed/required/used/measured/harvested'; and
- 'Left anterior descending/LAD'.

The articles were then manually screened for empirical measurements of the IMA lengths used in in-situ grafting to the LAD via median sternotomy or minimally invasive techniques. Non-specific measurements of the IMA, free-grafts and re-operative CABGs were excluded as were non-English and duplicate references. In total, over 500 references and 100 full text articles were reviewed.

To explore other solutions to this dilemma, similar searches were conducted on the anatomy and clinical application of the IMAs in autologous breast reconstruction and CABG. The results identified were manually reviewed and selected based on their relevance to the present topic.


IMA length needed for CABG
Novel approaches to IMA based breast reconstructions
Anatomical study
315 Hemithoraces
Literature review
>500 references & 100 full text articles
Literature review
Clinical uses of IMAs in autologous breast reconstructions and CABG
Cadaveric component
75 Hemithoraces
Clinical component
240 Hemithoraces
Median sternotomy
5 Articles
1019 IMAs
Minimally invasive CABG
6 Articles
555 IMAs
Length of IMA at each ICS
Length of IMA needed for CABG
Results
Clinical and laboratory data on IMA perforators and retrograde flow
ICS at which a sufficient length of IMA can be preserved for CABG
Alternative techniques for preserving the IMAs
Technique 2: IMA perforators
Technique 3: End-to-side anastomosis
Technique 4: Use of the DIEA pedicle
Technique 5: Retrograde DIEP
Technique 1: lowering the DIEP flap to preserve the IMAs for future CABG
Review of techniques for preserving the IMA for CABG
Total of 5 techniques identified

Results

Anatomical Study

Measurements of the IMAs at each ICS from the 315 hemi-thoracic walls are shown in Table 4. On average, the RIMA (177·80mm+/-44·3mm) was shorter than the LIMA (186·90mm+/-37·5mm) and bifurcated at a higher level. Specifically, 26% of RIMAs measured bifurcated at the 5th ICS and the rest at the level of the 6th rib. In contrast, 16% of the LIMAs bifurcated at the 5th ICS, 73% in the 6th ICS and 11% in the 7th ICS.

The IMA diameter at each ICS decreased progressively as the IMA descended caudally and exhibited little difference between each side (Table 4). The mean diameters of the LIMA and RIMA were 2·8mm/2·8mm (2·1-3·6mm) at the inferior border of the clavicle and 1·7mm/1·8mm at the bifurcation.

The size and number of IMAPs exhibited a similar pattern, decreasing from an average size of 1·4-1·5mm in the first two ICS to 0·6-0·9cm in the lower three ICS' (Table 5). The presence of perforators >1mm was present in 87% and 91% of patients in the first two ICS, but only 3% by the 6th ICS.

Literature Review

From the review on the IMAs, 11 studies quoted exact lengths of the LIMA needed to graft the LAD and are shown in Table 4 [70-81] Of these, five used open harvesting techniques (n=1019) and six employed minimally-invasive techniques (n=555). The mean lengths weighted according to sample size were 160·08mm and 152·70mm respectively, and correspond anatomically to the level of the 4th rib.

The exact length of the RIMA required for CABG was inconsistently reported as it depended to a large degree on the arteries bypassed and type of anastomosis used. The bulk of the literature that we reviewed harvested the RIMA from its bifurcation (177·80mm in our study) and trimmed it to the required length intraoperatively. For the purposes of discussion, we use this more conservative figure to err on the side of safety. Further, we discuss the DIEP pedicle, IMA perforators and the retrograde limb of the IMA as the most relevant and novel approaches of using the IMA for DIEP flaps and CABGs.

Discussion

Comparing the anatomical features of the in-situ IMAs at each ICS will assist in bridging an elusive gap between reconstructive and cardiothoracic techniques. Based on the results of our study and literature review, there are five methods of modifying the DIEP to allow future reuse of IMA for CABG.

Technique 1: Lowering the Site of DIEP Anastomosis

Our anatomical study (Table 4), shows the ICS' at which DIEP reconstructions can be safely performed to preserve these IMA lengths for pedicled grafting to be the 5th for the left and 6th on the right. If the IMAs are harvested in a skeletonised fashion, the additional length gained permits DIEP reconstructions to be anastomosed one level higher in the 4th and 5th ICS' (Figure 5). These conclusions correlate well with the only other study on this technique which also supports the 4th and 5th ICS as being suitable for leaving a sufficient length of IMA for future CABG [15]. Some surgeons have raised concerns regarding the diameter of the IMA below the 4th ICS and that the 5th-7th costal cartilages are very narrow and sometimes fused. Our study indicated that the mean diameter of the LIMA was 2.0mm (1.2-2.6) at the 4th ICS which is sufficient for an end-to-end anastomosis. The RIMA was also of sufficient calibre, averaging 1.8mm (1.2-2.4) at the 5th ICS. A standard rib resection or minimally invasive approach can be used to access the IMA should the interspaces be narrow [82].

The main limitation of this technique is the relative inconsistency of the internal mammary vein (**IMV**) below the 3rd ICS. The IMVs are almost universally present and accompany the IMA as they descend caudally lateral to the sternum. However, around 70% of IMVs (types 1 and 3) bifurcate by the 4th rib to form two vessels of reduced internal diameter [83]. Accordingly, there is a significant degree of variability in the diameters available for anastomosis at the 5th ICS (1·0-3·9mm), creating a degree of uncertainty regarding the availability of adequate venous drainage at that level [83]. This is an understandable concern to surgeons as venous congestion is a major cause of flap failure, complicating up to 10% of conventional DIEP reconstructions with up to 5% requiring reoperation [84-87]. Fortunately, the majority of IMVs at this level are of suitable calibre (1·7-2·5mm) and can be accurately assessed through radiological means. Although this technique may not be an option for every patient, suitable candidates can be readily identified through careful preoperative imaging. If the IMVs are small, then it is important to consider the superficial epigastric veins (SIEVs) [84, 86, 88-90]. Flap congestion has been noted to occur when the SIEV exceeds 1.5mm in diameter as this is postulated to be associated with inadequate venous communication between the two systems [86, 91]. Therefore a popular solution for overcoming venous complications takes the form of routinely exposing the SIEV when raising the DIEP flap for either prophylactic creation of an additional venous outflow or as a 'lifeboat' for salvaging congested flaps in the post-operative period [84, 91-94]. The SIEV can then be anastomosed to augment the blood flow from the superficial to deep systems to the DIEV or its vena comitantes, or as an alternative outflow to other venous networks such as the IMV (retrograde limb or perforator vessels) [95, 96], lateral thoracic, thoracodorsal, circumflex scapula, intercostal, cephalic or basilic veins. Regardless of the choice of anastomosis, there is some evidence that the use of an additional venous outflow option can reduce the incidence of flap congestion without affecting flap survival or operating time [84, 90].

Technique 2: Using IMA perforators

Several studies have suggested that DIEP flaps can be anastomosed to IMAPs to spare the IMA proper for future use in CABG [9, 12-14, 31-33, 97, 98]. The additional advantages of using IMAPs compared to the IMAs include avoidance of the need to excise the ribs or costal cartilage in order to gain access the IMA, and in doing so also minimises operating time, post-operative pain, pulmonary complications and contour deformities. (TABLE 2) [13, 14, 31, 99, 100]. The disadvantages of IMAPs centre on concerns over their reliability, availability, calibre and venous drainage. These factors have limited the widespread uptake of IMAP as recipient vessels however new studies are now clarifying much of the uncertainty surrounding this technique. Recent clinical series by Follmar et al [13] and Saint-Cyr et al [32] have both shown that with careful patient selection and adequate clinical experience, DIEP flaps can be safely anastomosed to IMAPs without increasing the incidence of flap loss or fat necrosis compared to the IMA or thoracodorsal vessels. Several studies, this study included, show that such a procedure is anatomically feasible in the majority of women given the high incidence of usable perforators in the 1st and 2nd ICS (87-91%) [12, 33]. Interesting however, the proportion of breast reconstructions with suitable IMAPs reported range from 9% to 39% depending on the institutional selection criteria (Table 7) [12-14, 31, 32, 98]. A major factor limiting the uptake of IMAPs is perforator damage during mastectomy and/or radiotherapy. If the breast surgeon is vigilant, this should not be a problem, and in selected cases, a more proximal segment of the undamaged IMA or an interspace spared radiation may be used [14, 32]. As with any new procedure, a learning curve exists within the surgical unit and uptake rates increase with the number of DIEP-IMAPs performed. A prospective study of 100 consecutive DIEP flaps clearly demonstrated increasing IMAP rates with every 20 reconstructions performed, as IMAP vessels were increasingly spared by the general surgeons during mastectomy and used for subsequent reconstruction. By the end of this study, an utilisation rate of 45% (n=9/20) was achieved without a statistical increase in the number of complications [13].

In terms of IMAP calibre, previous studies have reported values of between 1.0mm and 1.83mm with the largest or ‘principle’ perforator lying in the 2nd or 3rd ICS (Tables 7 & 8)[12-14, 31-33, 101]. This is in keeping with our findings which show the highest incidence of usable perforators (>1mm) to be in the 2nd ICS (91%) with a mean internal diameter of 1.5mm (0.9-2.5mm) on the right IMA and 1.6mm (0.9-2.9mm) on the left. Any mismatch between the DIEP pedicle and the IMAP can be overcome via traditional microsurgical techniques. Our analysis of 315 hemithoracics is the largest study to date and all measurements were accurate to 0.1mm.

Some authors have expressed concern over the venous drainage of DIEP-IMAP reconstructions. Given the aforementioned rates of venous complications in conventional DIEP flaps, it is understandable therefore to assume that DIEP-IMAP flaps may experience at least an equivalent if not higher rate of venous inadequacy given the smaller calibre of perforator vessels. However this does not appear to be the case in the studies to date and intra-operative measurements by Saint-Cyr et al found that IMV and IMVP have similar diameters (2.8mm vs 2.9mm) after reversing vessel spasm and mechanical dilation [32]. Furthermore, DIEP-IMAP flaps can be supercharged with additional venous outflows as described in Technique 1.

Using our review of the cardiothoracic literature, we propose two ways in which a ‘DIEP-IMAP’ flap can be performed to preserve the IMA for CABG. First, it may be possible to separate the IMAP from its parent vessel after a period of delay in the process of skeletonising the IMA for CABG (Figure 6a). The advantage of this method is that it enables IMAs to be harvested through a standard cardiothoracic technique without a need for increased operating time. Alternatively, the LIMA may be harvested without disconnecting the DIEP-IMAP (Figure 6b) by skeletonising the LIMA from the level of the flap, beyond its bifurcation, to the first 2-3cm of the DSEA, a technique similar to harvesting an extended RIMA for grafting to non-LAD arteries. This method may permit both the DIEP and LAD to be perfused with the same IMA.

Technique 3: End-to-side anastomosis of the DIEP flap to the IMA

End-to-side arterial anastomosis is a well described technique in microsurgical free flap reconstructions and has been shown to be as consistent and reliable as traditional end-to-end anastomosis in both clinical and experimental studies [10, 11, 102-107]. A recent series by Apostolides et al comparing 15 end-to-side anastomosis with and equivalent number of end-to-end anastomosis in 30 consecutive DIEP and SIEA reconstructions demonstrated that that the only statistically significant difference between the two techniques was longer ischemia in the end-to-side group (20 minutes) [10]. These were not associated with increased flap complications or the no-reflow phenomenon.

Technique 4: Using the DIEP Pedicle as a Composite Graft

Recent studies have shown that the average DIEP pedicle processes a similar diameter to the IMA (2·0-3·6mm vs. 1·7-2·8mm) [108]. Therefore, if a CABG is necessary, a segment of the DIEP pedicle can be used as a composite graft to obtain the length required (Figure 7). In fact, the DIEP’s parent vessel, the inferior epigastric artery, has been used as a composite graft with excellent patency rates (85% over 81 months), possibly due to the downstream effect of cytokine secretion by the IMAs [38, 109]. The advantage of this method is that it enables women with pre-existing DIEP flaps to receive IMA based CABGs if needed. To facilitate this, reconstructive surgeons should aim to harvest the DIEP in its entirety (8-15cm) and tunnel the pedicle to the anastomotic site to minimise handling of the IMA [108]. Most patients with pre-existing DIEP flaps are amenable to this technique and the patency of the DIEP pedicle can be imaged pre-operatively to assess patency and flow rates prior to CABG.

Technique 5: The Retrograde DIEP Flap

Retrograde flow from the distal limb of the IMAs has been used on rare occasions for CABG and salvage of breast reconstructions with compromised arterial supply [110, 111]. Historically, studies from the 1980’s intra-operatively measured the retrograde flow from the distal IMA to be as high as 60ml/min [110]. Retrograde CABGs however did not become mainstream due to the unpredictable and highly variable vascular anatomy between individuals. Now, advances in imaging technology enable surgeons to accurately visualise anatomical variations. Therefore we hypothesise that under the guidance of careful preoperative imaging, a ‘retrograde DIEP’ flap anastomosed to the distal IMA may be a feasible recipient vessel for DIEP flaps in select individuals

(Figure 8), especially as the distal limbs of the IMV have also been used successfully as an outflow option for DIEP flaps.

To 'retrograde DIEP flap' isuntested although personal experience of some surgeons suggest that this anastomosing the DIEP flap in a retrograde fashion is not always predictable and often requires a need to maintain a mean systolic pressure of above 130mmHg; and is therefore a suboptimal strategy in women with strong cardiovascular risk factors. Nonetheless, further investigations are warranted as this approach may preserve the operative field entirely undisturbed for future CABG Further and importantly, the metabolic requirements needed to support a DIEP flap are unlikely to be as demanding as those of a coronary artery to which the distal IMA has already been successfully grafted.

Impact of Findings

The findings of this paper support the theory that using the IMA for autologous breast reconstruction is not an absolute contraindication for CABG as there are a number of procedures which can be used to accommodate high risk patients. The optimal techniques for reconstruction following mastectomy and coronary artery bypass grafting are not necessarily mutually exclusive and impacts two major patient populations: women who require reconstruction after bilateral mastectomy (10% and growing), and women who derive a survival benefit from BIMA which, pending results of current trials, may be the majority of CABG candidates. The full impact of these findings is likely to be under-appreciated due to the age gap between the two conditions (Figure 2), the projected increase in both conditions and the fact that current statistics on breast reconstruction exclude women turned away from DIEP flaps for fear of its prohibitive effect on future heart surgery. The concepts brought forward in this paper aim to catalyse further discussion and collaboration between cardiothoracic surgeons and plastic surgeons, to potentially improve women's health.

TABLE LEGENDS

Table 1: The rates of breast cancer, mastectomy and coronary artery bypass graft procedures performed per 100,000 population in the top 25 countries of the Organisation for Economic Co-operation and Development (OECD) in 2010.

Table 2: Comparison of the advantages and disadvantages of the common recipient vessels for autologous breast reconstruction. The reliability, medial position and superior blood flow makes the internal mammary artery (**IMA**) an ideal recipient vessel for autologous reconstructions. The main drawback of using the IMA for this procedure is that it prohibits future coronary artery bypass grafting from being performed.

Table 3: Comparison of the advantages and disadvantages of the common conduits used for coronary artery bypass grafting. The internal mammary artery is currently the gold standard conduit, by virtue of its superior long term patency and proven survival benefit over other grafts.

Table 4: Anatomical features of the internal mammary arteries (**IMAs**) with lengths and diameters measured at each intercostal space. Note that no measurement for the sixth intercostal space (**ICS**) is given for the right IMA, as the IMA bifurcated at or before the sixth rib. In contrast, bifurcation of the left IMA most commonly occurred in the sixth ICS. The 'origin' of the IMA was measured from the lower border of the clavicle.

Table 5: Presence and diameter of internal mammary artery perforators (**IMAPs**) at each intercostal space (**ICS**). Note the high percentage of patients with usable IMAPs (>1mm) in the first two ICSs, making these the most reliable levels for autologous breast reconstruction. (IMA = internal mammary artery.)

Table 6: Lengths of internal mammary arteries (**IMAs**) required for coronary artery bypass grafting (**CABG**) to the left anterior descending artery (**LAD**), as quoted in the literature. The IMA lengths stated are measured in millimetres (mm). (LIMA = Left internal mammary artery. RIMA = Right internal mammary artery.)

Table 7: Clinical studies which have utilised the internal mammary artery perforators as recipient vessels in autologous breast reconstruction as a means of sparing the internal mammary artery for coronary artery bypass grafting. (DIEP = Deep inferior epigastric artery perforator flap. SGAP = Superior gluteal artery perforator flap. SIEA = Superficial inferior epigastric artery flap. TRAM = Transverse rectus adominis myocutaneous flap. MS-TRAM = Muscle sparing TRAM.)

Table 8: Anatomical studies that have investigated the presence and diameter of internal mammary artery perforators for the purpose of assessing its suitability as a recipient vessel in autologous breast reconstruction. The sample size of our anatomical study is the largest to date and is accurate to within 0.1mm.

FIGURE LEGENDS

Figure 1: Summary of the advantages and disadvantages of the most common methods of post-mastectomy breast reconstruction. Notably, the deep inferior epigastric artery perforator flaps delivers more superior aesthetic appearance and carries a lower risk of donor site morbidity than alternative options available.

Figure 2: Incidence of coronary artery bypass grafts and breast reconstructions performed, by age, in the United States. Significantly, there is a twenty year delay in the peak incidence between the two procedures.

Figure 3: X-ray angiogram of the internal mammary arteries (**IMAs**) at each intercostals space, illustrating the course of the IMA and the reference points from which diameters and lengths were measured. (DSEA = deep superior epigastric artery.)

Figure 4: Internal mammary arteries as seen by computed-tomographic angiography.

Figure 5: A deep inferior epigastric artery perforator flap that is anastomosed at the fifth intercostal space leaves a sufficient length of the internal mammary artery for direct reuse in coronary artery bypass grafting.

Figure 6: Two methods of performing coronary artery bypass grafting options for a deep inferior epigastric artery perforator (**DIEP**) flap that is anastomosed to the internal mammary artery perforators at the second intercostal space. Figure 6a shows the separation of the DIEP flap during harvesting of the internal mammary artery. Figure 6b shows the DIEP flap left in-situ for shared perfusion with the left anterior descending artery.

Figure 7: The deep inferior epigastric artery perforator (**DIEP**) pedicle can be used to extend the internal mammary artery for coronary artery bypass grafting in patients with conventional DIEP flaps anastomosed at the 3rd intercostal space.

Figure 8: A deep inferior epigastric artery perforator flap that is anastomosed to the retrograde limb of the internal mammary artery (**IMA**), leaving the proximal IMA undisturbed for coronary artery bypass grafting.

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Table 1: The rates of breast cancer, mastectomy and coronary artery bypass graft procedures performed per 100,000 population in the top 25 countries of the Organisation for Economic Co-operation and Development (OECD) in 2010.

Country	Breast cancer[17]	Country	Mastectomy[18]	Country	CABG[18]
Belgium	109·19	Finland	89·0	Germany	131·8
Denmark	101·12	Belgium	87·0	Belgium	131·4
France	99·74	Netherlands	84·0	United States [2006]	84·5
he Netherlands	98·46	Denmark	83·0	Norway [2006]	81·0
Israel	96·77	Sweden	81·0	Denmark	80·5
Iceland	95·52	Korea	72·0	New Zealand	77·5

Vessel	Advantages	

Ireland	93·94	Australia	71·0	Australia	71·8
Switzerland	89·38	Germany	70·0	Italy	70·7
New Zealand	89·37	Norway	70·0	Canada	68·9
nited Kingdom	89·13	Luxembourg	68·0	Slovenia	62·8
Finland	86·31	United Kingdom	68·0	Czech Republic	62·4
Italy	86·29	France	61·0	Luxembourg	61·3
Australia	84·75	Switzerland	59·0	Iceland	59·7
Canada	83·17	Canada	54·0	Netherlands	58·2
Luxembourg	82·35	Austria	53·0	Finland	57·7
Germany	81·76	Italy	53·0	Israel	56·5
Sweden	79·40	New Zealand	51·0	Sweden	56·4
United States	75·99	Portugal	51·0	Poland	52·6
Norway	73·50	Israel	48·0	Austria	51·6
zech Republic	70·85	Slovenia	46·0	United Kingdom	45·7
Slovenia	64·87	Iceland	45·0	Portugal	43·0
Croatia	63·99	Ireland	45·0	Ireland	40·5
Austria	62·13	Spain	45·0	Hungary	36·3
Spain	61·01	Hungary	43·0	France	30·9
Portugal	60·02	United States[2006]	40·0	Switzerland	30·8
CD AVERAGE	**83·2**	**OECD AVERAGE**	**61·5**	**OECD AVERAGE**	**64·2**

Internal mammary artery	• Eliminates the need for axillary dissection and potential risk of lymphoedema and nerve damage [9] • Larger diameter and superior flow compared to the thoracodorsal vessels [9, 112] • Consistent location that is easy to access via microsurgical means. Good positioning for surgeon and assistant [14, 113, 114] • Requires a shorter pedicle than axillary vessels for anastomosis [14, 115] • Medial location of vessels allows for more flexible flap placement and superior shaping of the breast mound, especially with smaller flaps [14, 113, 115-117]	• Respiratory movement • Risk of pneumothorax and post- • Need for rib resection may caus this can be avoided via an interc Other minimally invasive appro • Precludes future CABG with IM
Thoracodorsal artery	• Easy access in patients who are undergoing axillary lymphadenectomy as the axilla is already exposed [14] • Consistent anatomy and adequate diameter, especially at the level of the serratus branch [14, 119] • Commonly used recipient vessel with proven reliability [14, 83, 116, 120, 121] • Does not preclude future CABG	• Primary axillary dissection for b increasing utilisation of sentinel expose the thoracodorsal vessel • Thoracodorsal vessels are frequ post-operative radiotherapy mak the incidence of unusable vesse 119] • Limits the options for re-operati tumour recur as the pedicled lat are also based off the thoracodo • Patient position required for mi them to reach across the chest [1 • Aesthetically inferior to the IMA and axillary scarring [114] • Risk of pedicle avulsion and sh
Circumflex scapular artery	• Large arterial and venous diameters (1.5-3mm) are favourable for microanastamosis to the DIEP pedicle [121] • Rarely damaged by previous surgery or irradiation [14, 121] • Does not preclude future CABG	• Patient position required for mi them to reach across the chest [1 • Medial placement of the breast a common problem[114]
Internal mammary artery perforators	• Decreased operative time to expose IMAPs as compared to the IMA and thoracodorsal vessels [9] • Less invasive dissection reduces post-operative discomfort [14] • IMAPs in the 1st and 2nd ICS may be free from irradiation or previous surgery [14] • Avoids need to resect costal cartilage and risk of thoracic deformity [9, 14] • Superior positioning for both the surgeon and assistant [9, 14] • Shown to be a safe and reliable recipient site for anastomosis in selected patients [10, 12-14, 32, 98] • Spares the IMA for future CABG [9, 14]	• Smaller calibre vessels create u 101] • Thin walled veins [14] • Technically demanding procedu • Suitable IMAPs are not always during mastectomy depending

Table 2: Comparison of the advantages and disadvantages of the common recipient vessels for autologous breast reconstruction.

Table 3: Comparison of the advantages and disadvantages of the common conduits used for coronary artery bypass grafting.

Conduit	**Advantages**	**Disa**
	• Superior long term patency [38, 44, 45] *1 year – 93-99%* *5 year – 88-100%* *10 year – 90-95%*	• Currently precludes IMA autologous breast reconst • Limited length available f

Internal mammary artery	*15 year – 85-92%* • Proven survival benefit [38, 48, 122] • Superior survival rates compared to saphenous vein grafts [123] *1 vessel disease — 93 versus 88 percent* *2 vessel disease — 90 versus 80 percent* *3 vessel disease — 83 versus 71 percent* • Relatively immune to atherosclerosis [38-40]	
Saphenous vein	• Easily accessible [122] • Adequate length to access every coronary vessel [122] • Correct diameter for coronary and aortic anastomosis [122]	• Impaired ambulation [122 • Limiting factor in surviva saphenous vein grafts [38]. • Inferior patency rates con *1 year – 78-86%* *5 year – 65-82%* *10 year – 57-61%* *15 year – 53%* *20 year – 20%*
Radial artery	• Available as a free graft [38] • Good length (>20cm) and diameter (2-3mm) [122] • Technically less demanding due to thicker muscular wall [122] • Can be harvest concurrently with other conduits [122] • Adapted to higher arterial pressures [122] • Good long term patency after first post-operative year [126]	• Prone to intimal hyperpla • Muscular artery; prone to • Contraindicated in ulnar a raynauds disease and arte • Inferior patency rates con *1 year – 51-90%* *5 year – 83-91%* *10 year – 83%*
Gastro-epiploic artery	• Good short term patency [38, 122] • Reliable donor when other conduits are scarce	• Thick smooth muscle me • Inferior patency rates con *2 year – 88%* *5 year – 86-90%* *10 year - 67%* • Fragile, increased operati complications such as dis

Table 4: Anatomical features of the internal mammary arteries with lengths and diameters measured at each intercostal space.

	RIGHT				LEFT			
	Length (mm)		**Diameter (mm)**		**Length**		**Diameter**	
	Mean	Range	Mean	Range	Length	Range	Mean	Range

Origin	-	-	2·8	2·1-3·6	-	-	2·8	2·2-3·5
1st ICS	54·9	44-69	2·6	2·1-3·2	58·7	42-74	2·6	2·0-3·2
2nd ICS	88·1	75-118	2·4	1·6-3·1	92·9	72-119	2·4	1·7-3·1
3rd ICS	119·1	100-156	2·1	1·4-2·8	121·1	101-156	2·1	1·5-2·8
4th ICS	148·5	120-188	1·9	1·3-2·5	148·9	121-190	2	1·2-2·6
5th ICS	170·8	142-210	1·8	1·2-2·4	167·1	139-208	1·8	1·2-2·5
6th ICS	-	-	-	-	182·1	161-202	1·7	1·4-2·5
Bifurcation	177·8	132-233	1·8	1·1-2·3	186·9	150-225	1·7	1·0-2·5

Table 5: Presence and diameter of internal mammary artery perforators at each intercostal space.

	RIGHT			**LEFT**		
	Presence of perforating branch of the IMA > 1mm in diameter	**Perforator diameter (mm)**		**Presence of perforating branch of the IMA > 1mm in diameter**	**Perforator diameter (mm)**	
		Mean	Range		Mean	Range
1st ICS	87%	1·4	0·8-2·1	88%	1·4	0·8-2·5
2nd ICS	91%	1·5	0·9-2·5	92%	1·6	0·9-2·9
3rd ICS	65%	0·9	0·5-1·8	70%	0·9	0·5-2·8
4th ICS	6%	0·6	0·3-1·5	13%	0·6	0·3-1·4
5th ICS	5%	0·6	0·3-1·3	9%	0·6	0·3-1·0
6th ICS[3]	-	-	-	3%	0·5	0·3-1·0

Table 6: Lengths of internal mammary arteries required for coronary artery bypass grafting to the left anterior descending artery, as quoted in the literature.

STUDY	YEAR	LIMA-LAD	N
Median sternotomy			
Calafiore A et al [70]	1998	161.00	14
		177.00	14
Deja M et al [71]	1999	170.00	287
		177.00	70
Calafiore A et al [72]	1999	164.00	304

Bonacchi M et al [57]	2005	142.00	310
Gwozdziewicz M [75]	2008	166.90	20

udy	Year	n	Suitable cases	Mean vessel diameter	ICS used	Flaps performed	Flap necrosis	Fol [m
et al [14]	2003	30	9.0%	Artery = 1.0mm (0.5-1.3) Vein = 1.7mm (1.0-3.0)	2nd = 30% 3rd = 70%	DIEP = 26 SGAP = 3 SIEA = 1	3.3%	
d et al [125]	2003	21	39.0%	-	2nd & 3rd	DIEP, SGAP, SIEA	0%	
et al [98]	2003	5	-	Artery = 1.56mm (1.2-2.5) Vein = 1.4mm (1.0-2.2)	- -	TRAM	20%	(
z et al [12]	2004	40	32.5%	-	-	DIEP = 38	0%	
vr et al [32]	2007	38	27.0%	Artery = 1.9mm (1.5-2.0)	2nd = 41%	MS-TRAM = 12	1%	

Minimally invasive CABG [MICABG]			
Boonstra P et al [76]	1997	140.00	20
Lazarra R et al [77]	1999	153.00	16
		143.00	10
Zenati M et al [78]	1999	150.00	27
Cremer J et al [79]	1999	150.00	205
Trehan N et al [80]	2000	156.00	267
Ishikawa N et al [81]	2007	162.00	10
Weighted average standard CABG		**160.08**	**1019**
Weighted average MICABG		**152.70**	**555**

Table 7: Clinical studies which have utilised the internal mammary artery perforators as recipient vessels in autologous breast reconstruction as a means of sparing the internal mammary artery for coronary artery bypass grafting.

Vein = 2.9mm (1.7-4.0) 3rd = 53% DIEP = 10

4th = 6% TRAM = 9

SIEA = 7

r et al [13] 20 0.2

Study	Year	n	IMAP present in 2nd or 3rd ICS	Mean vessel diameter
Park et al [98]	2003	5	-	Artery = 1.56mm (1.2-2.5)
				Vein = 1.4mm (1.0-2.2)
Munhoz et al [12]	2004	32	86%	Artery = 0.85mm (0.6-1.0)
Rosson et al [101]	2005	20	-	Artery = 1.14mm (0.3-2.7)
				Vein = 1.14mm (0.25-3.5)
Schmidt et al [33]	2008	20	95%	Artery = 1.3mm (0.4-2.9)
This study	**2011**	**315**	**91%**	**Artery = 1.27mm (0.3-2.5)**

Table 8: Anatomical studies that have investigated the presence and diameter of internal mammary artery perforators for the purpose of assessing its suitability as a recipient vessel in autologous breast reconstruction.

Figure 1

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Figure 1: Summary of the advantages and disadvantages of the most common methods of post-mastectomy breast reconstruction.

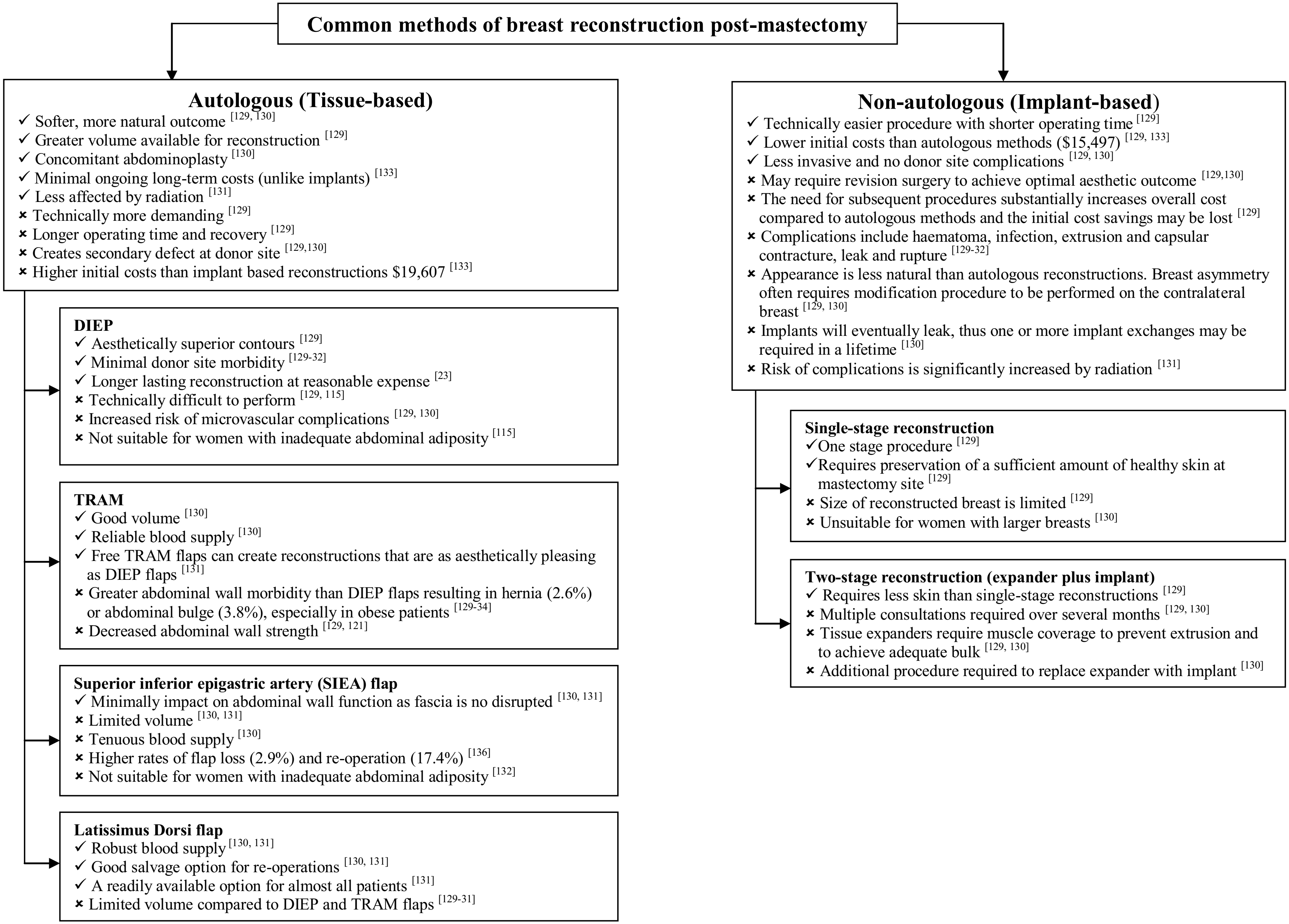

Figure 2
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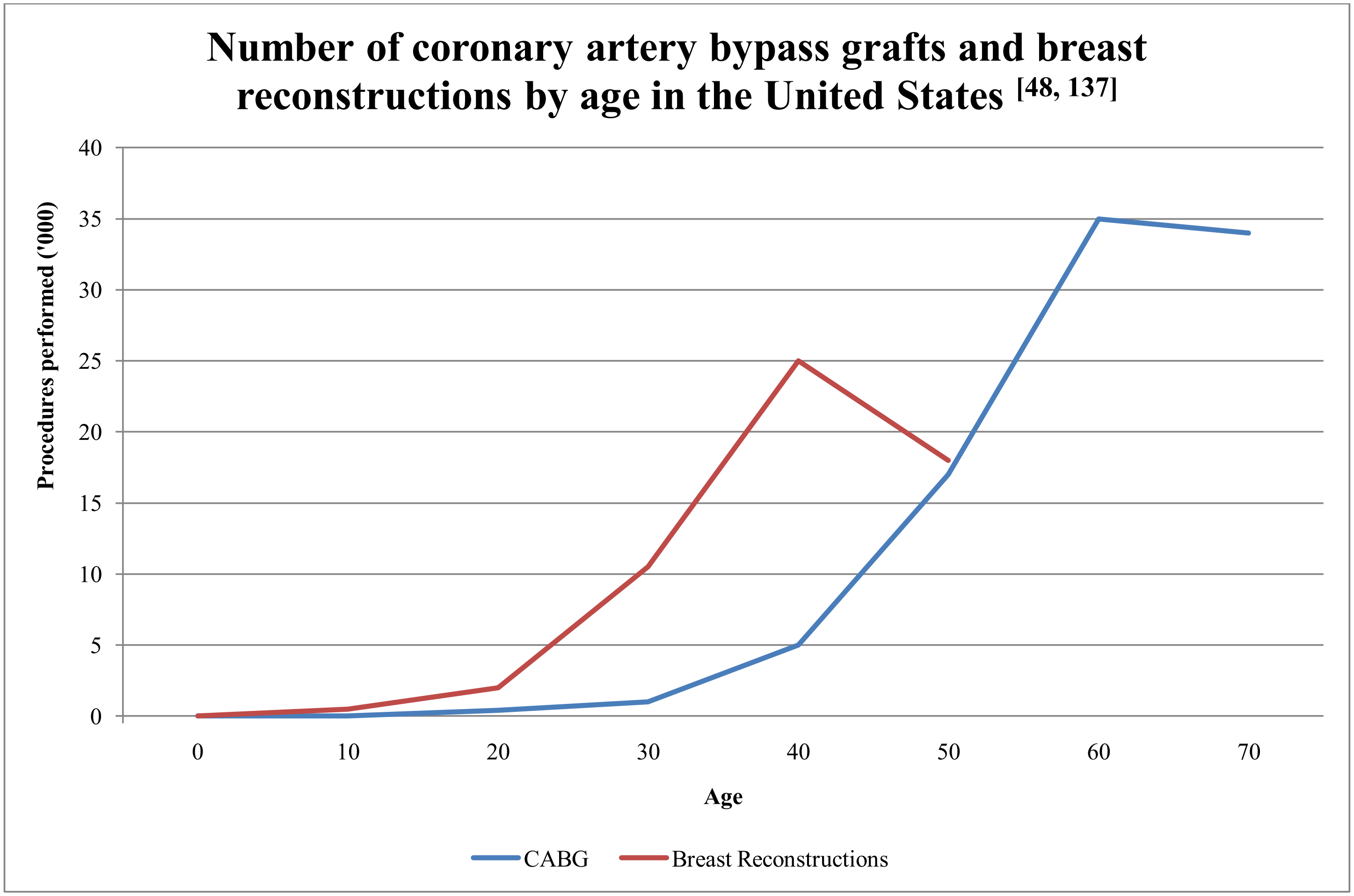
Figure 2: Incidence of coronary artery bypass grafts and breast reconstructions performed, by age, in the United States.



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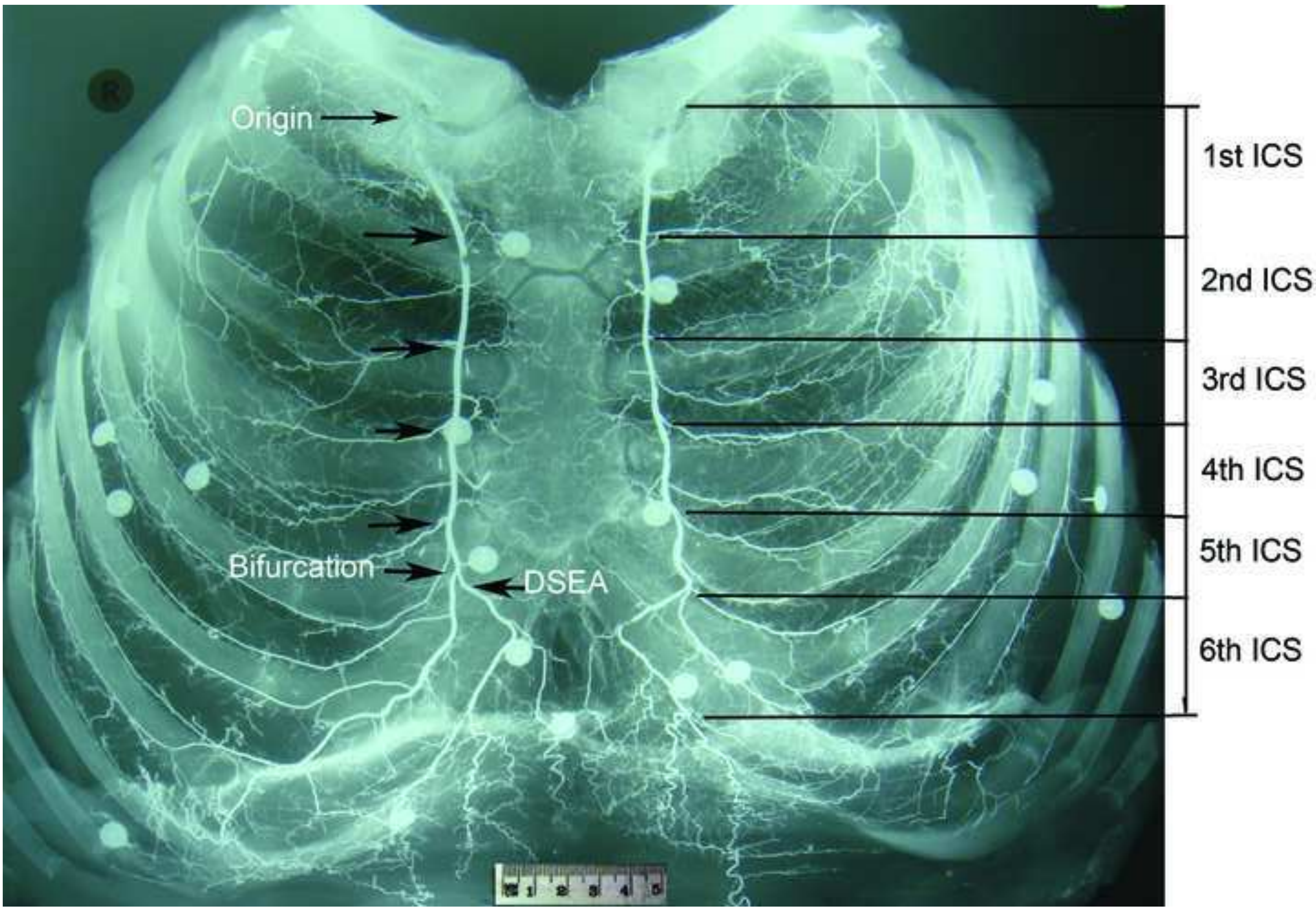

Figure 4

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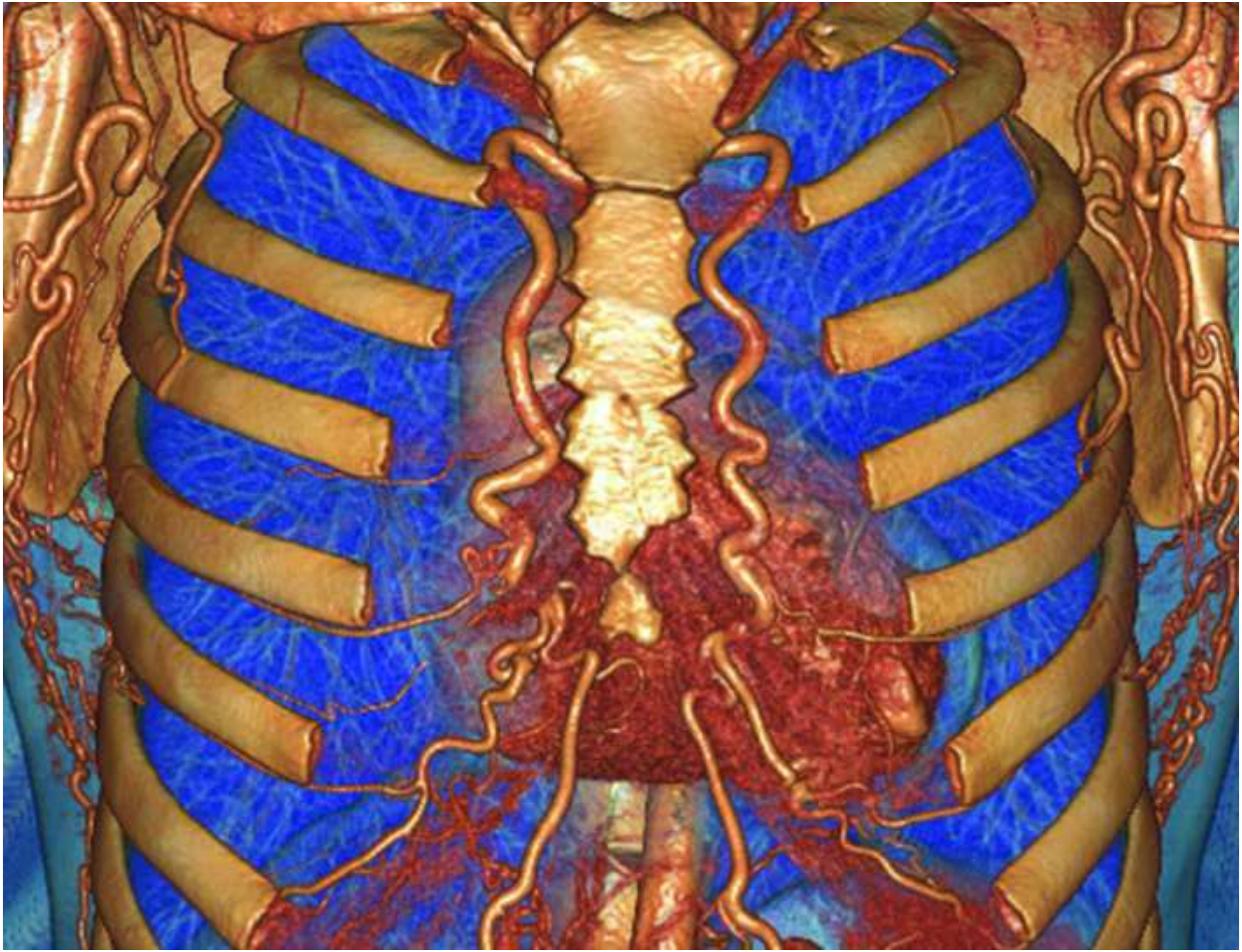

Figure 5

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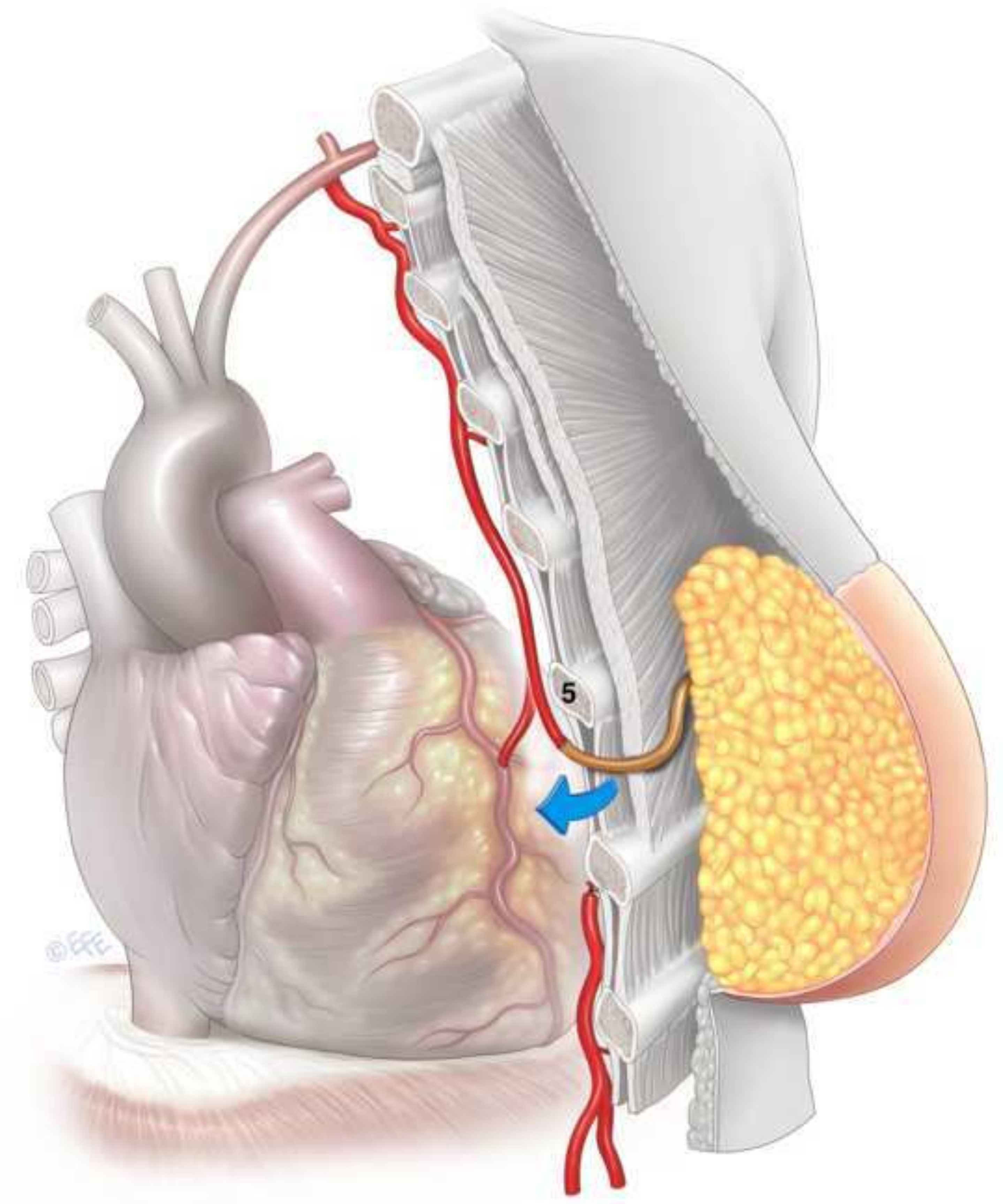

Figure 6

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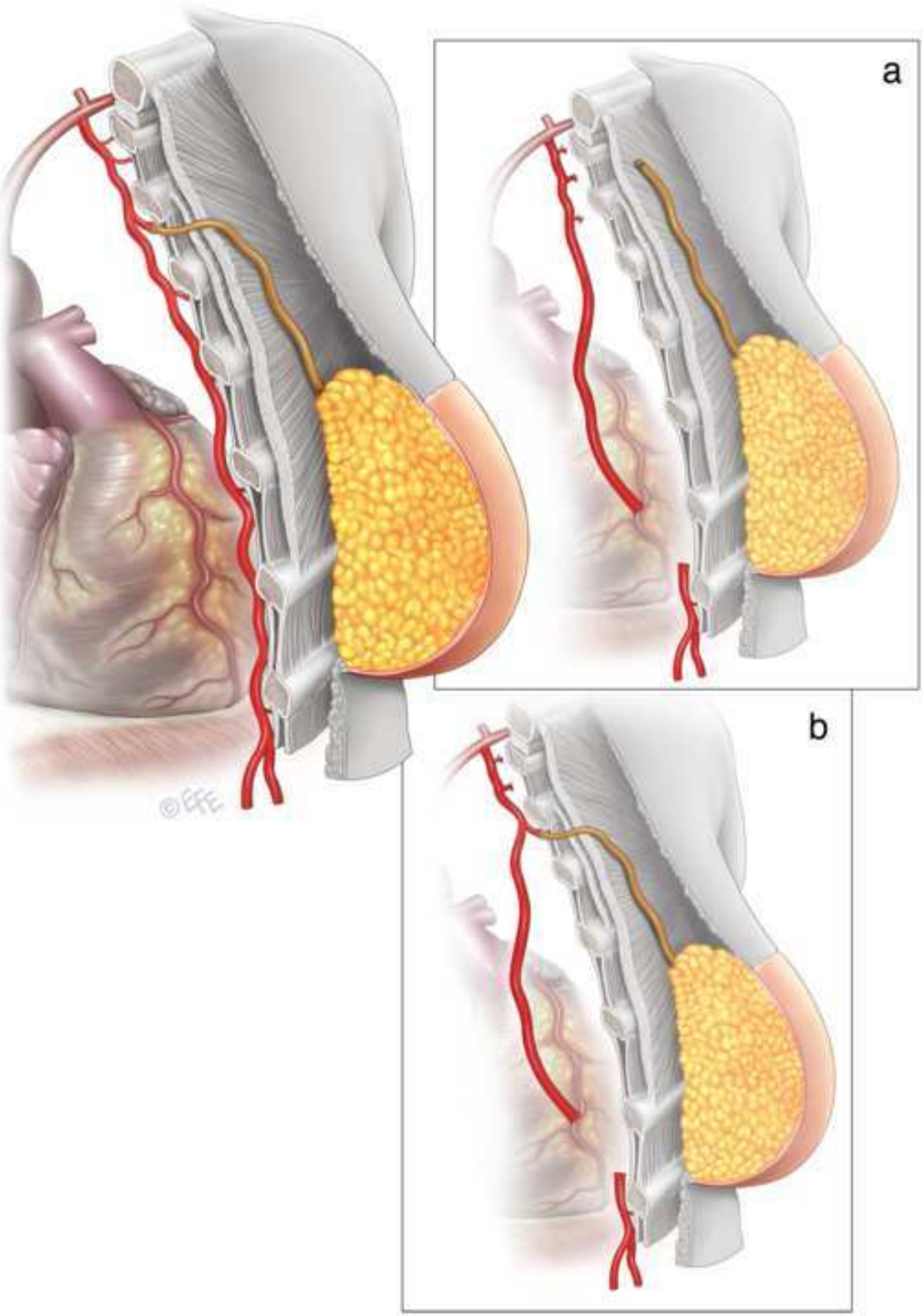

Figure 7

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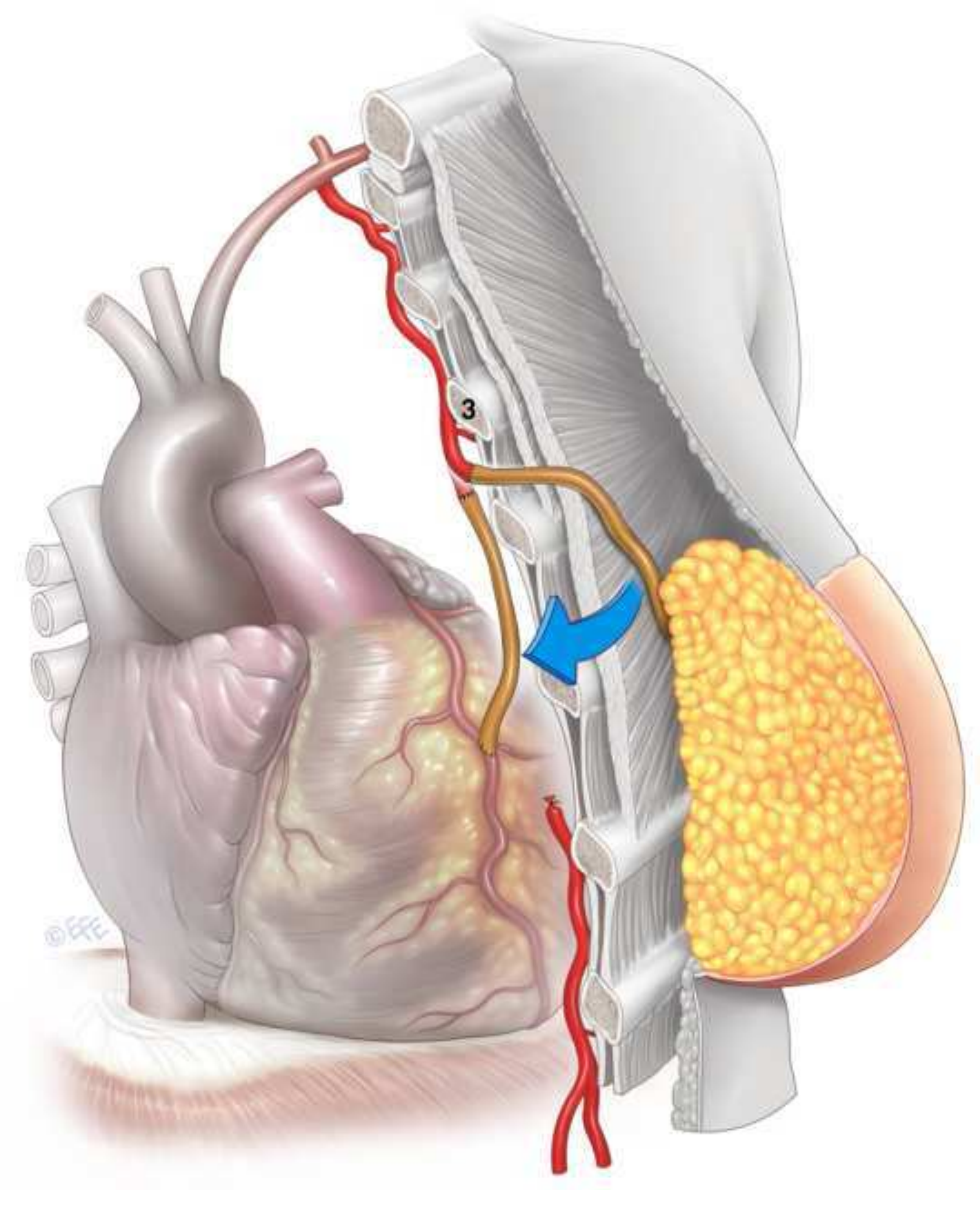

Figure 8
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