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Color Doppler ultrasound and computed tomographic angiography for perforator mapping in DIEP flap breast reconstruction revisited: A cohort study



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Summary *Introduction:* Preoperative imaging by Computed Tomographic Angiography (CTA) has been promoted a gold standard tool for perforator mapping in abdominally based microsurgical breast reconstruction, while Color Doppler Ultrasound (CDU) has lost its popularity. As the CTA X-ray exposure might have long-term consequences for patients, CDU has regained importance for preoperative workup in our center. Our aim was to revisit the role of CDU by comparing the reliability of CDU and CTA in predicting intraoperative perforator selection.

Materials and Methods: We performed a retrospective chart review study of patients who underwent microsurgical breast reconstructions with DIEP flaps at our institution. Both CTA and CDU were performed prior to the surgery, and both imaging entities were thoroughly examined by the surgical team. Perforator identification, number, size, and location were assessed and correlated with CTA and CDU data and with intraoperative findings.

Results: We identified 98 patients who received 125 DIEP flap surgeries. A significantly stronger correlation was found between CDU and intraoperative findings of perforator detection and size ($p < 0.0001$) and selection ($r = 0.9987$, CI 0.9981–0.9991, $p < 0.0001$ and $r = 0.01$, CI -0.18–0.2, $p = 0.91$, respectively), when compared with CTA data. If none of the preoperative imaging

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studies matched intraoperative perforator selection, an association with a higher incidence of flap loss (Odds ratio 4.483, CI 0.5068-39.65, $p=0.2171$) was found.

Conclusions: Our data suggests that CDU might regain relevance as a safe and reliable preoperative imaging study, without the risk and potential consequences of X-ray exposure. Preoperative imaging tools like CDU and CTA should be considered part of the gold standard in abdominally based free flap breast reconstruction.

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Introduction

Immediate breast reconstruction has become an integrated part of interdisciplinary breast cancer treatment and is associated with preservation of a woman's natural appearance, improved quality of life as compared to delayed or no reconstruction,¹ and the avoidance of a mastectomy trauma in patients already tormented by their cancer diagnosis.² The Deep Inferior Epigastric Perforator (DIEP) flap is considered the gold standard for autologous free flap breast reconstruction. This muscle preserving perforator flap technique led to a relevant reduction of abdominal morbidity,³ but is technically more challenging and time-consuming than a (Muscle Sparing) Transverse Rectus Abdominis Muscle (TRAM) flap due to the inconsistent anatomy of the abdominal perforators.⁴ To simplify and shorten DIEP harvest, different tools for preoperative planning have been applied and evaluated in the past. Color Doppler Ultrasound (CDU) is a safe yet operator-dependent, radiation free modality to define direct markings of perforators to the abdominal skin without the need for additional measuring systems. Computed Tomographic Angiography (CTA), on the other hand, is a fast and reproducible examination, allowing for visualization of the deep inferior epigastric artery (DIEA), its intramuscular course, and branching pattern.⁵ Despite X-ray exposure and (relatively low) risk of contrast toxicity, CTA has been promoted as a reference standard, whereas CDU has lost its popularity over the last decade, mainly due to interobserver variability.⁶ When comparing the two entities, the awareness of X-ray exposure is often neglected in favor of possibly better spatial representation of vascular anatomy. Radiation-induced cancer risk at an exposure level of >10 millisievert (msv) remains controversial, while an exposure level over 100 msv is a proven cancer inductor.⁷ A regular abdominal CT leads to an exposure of 10 msv. This might gain importance because prophylactic mastectomies have become more frequent, and consequently, a subgroup of this patient population has become younger.

Recent studies have also promoted Magnetic Resonance Angiography (MRA) as a nonionizing alternative to the CTA⁸ with a good contrast profile, but this examination is more expensive and time-consuming than CTA and CDU, and it bears the risk of motion artefacts leading to inferior quality and potentially negative implications for claustrophobic patients or metal porters.⁹ Newer propositions such as dynamic infrared thermography¹⁰ or laser-assisted indocyanin green fluorescent angiography (LA-ICGFA)¹¹ are promising mainly for intraoperative perfusion control, but less feasible for preoperative planning.¹²

In our cancer center, both CTA and CDU are routinely performed preoperatively for DIEP flap breast reconstruction. The aim of this study was to compare the accuracy of CDU and CTA regarding intraoperative perforator selection in DIEP flap surgery. Furthermore, we hypothesize that an intraoperative perforator selection mismatch of both CTA and CDU could potentially impact the risk of postoperative perfusion compromise.

Materials and methods

Imaging

CDU: All examinations were performed by one of two senior angiologists in a well-tempered room with an EPIQ 7 duplex device (Philips, Best, Netherlands), with either a linear 12-3 MHz or a 18-5 MHz transducer (depending on the depth of penetration and/or quality of the resolution). The sonographers documented the patency of the epigastric inferior artery from its origin, and followed and marked its course upward with the level of penetration through the visceral fascia by using a water-resistant pencil (Figure 1). All visible perforators and their main arborization into the subcutaneous tissue were also marked on the skin (Figure 2). The markings were followed by an immediate sonographic cross-checking to assure correct positioning. In case of excellent visualization, the diameter of the perforators, preferentially at the height of fascia penetration, was also measured. The senior surgeon joined the angiologist whenever possible at the end of CDU. During surgery, CDU markings were again verified by the surgical team. Intraflap branching, intramuscular course, and subcutaneous interconnections between superficial and deep inferior epigastric arteries and veins were also routinely marked by the angiologist.

CTA: CTA was performed with a standardized DIEP protocol and as a dose-adapted CT, resulting in a radiation exposure of 1.8-2.9 mSv. All examinations were performed on a dual-source multidetector scanner (MDCT) (Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany). We applied a standard-of-care imaging protocol with an x-ray tube voltage of 80 kVp, effective reference x-ray tube current of 250 mAs, and a gantry rotation time of 0.5 s for MDCT acquisition. Real-time angular dose modulation for the x-ray tube current (CareDose 4D, Siemens Medical Solutions, Forchheim, Germany) was activated. All cranio-caudal helical MDCT studies were reconstructed at 1 mm thickness with 0.5 mm reconstruction increment,

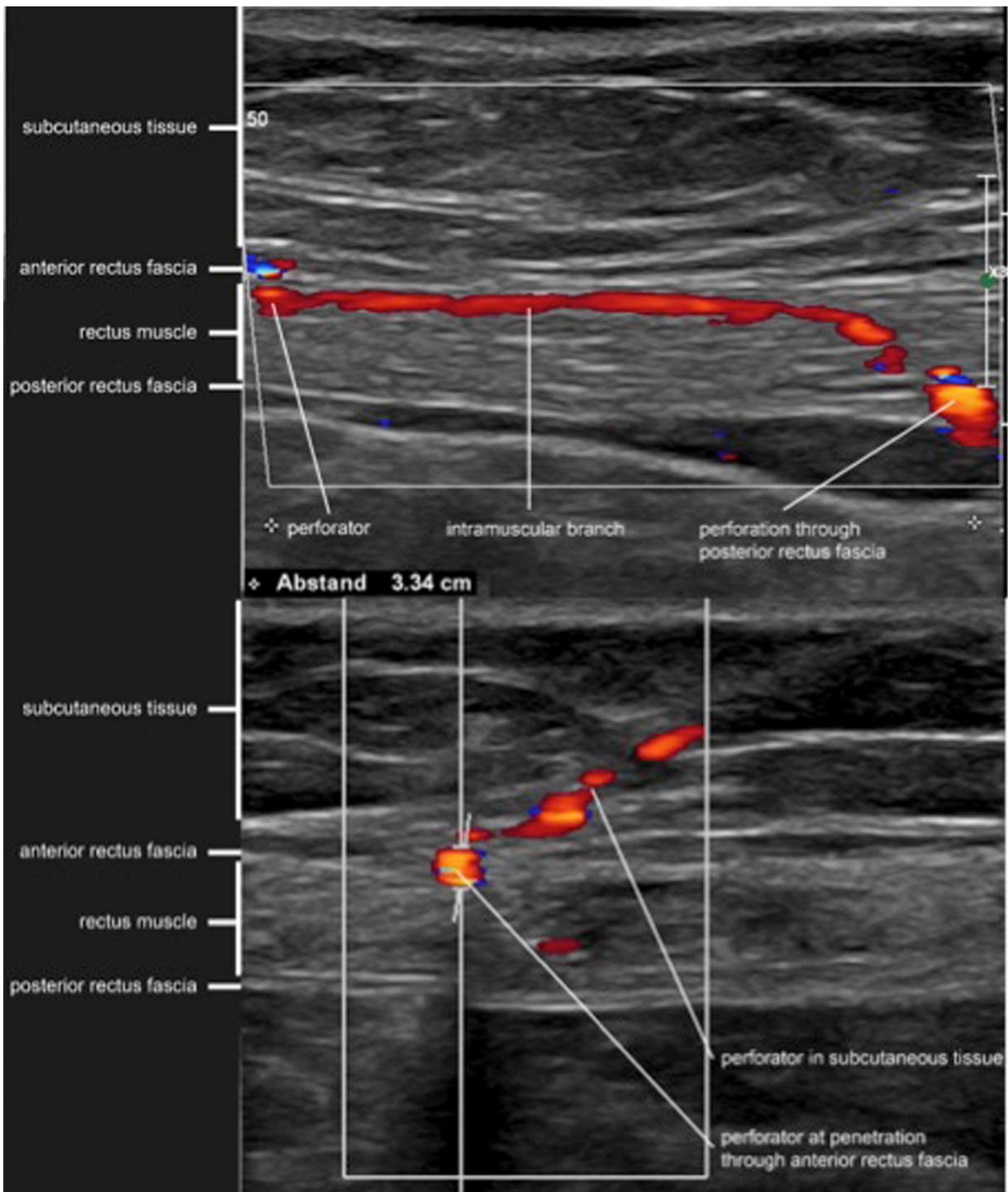


Fig. 1 CDU image. (A) Intramuscular course of the branch perforating at the anterior rectus fascia. (B) Measuring of perforator size at passage through the anterior rectus fascia.

using a hybrid iterative reconstruction (Sinogram Affirmed Iterative Reconstruction [SAFIRE], Siemens Medical Solutions, Forchheim, Germany) soft tissue kernel. For all patients, individual contrast bolus-tracking was performed during repetitive low-dose acquisitions at 120 kVp/40 mAs and placement of a threshold region-of-interest (ROI) within the abdominal aorta at the level of the bifurcation. Hounsfield Unit (HU) contrast wash-in to a level of

100 HU following 80 ml of contrast, iopamirol-350, was injected at 4 ml/sec chased by 50 ml of normal saline injected at the same rate into a right antecubital vein using a CTA dual injector after a preprogrammed constant diagnostic delay of 9 s. The diagnostic cranio-caudal helical MDCT study with a collimation of 128×0.6 mm was automatically initiated subsequently. Average radiation dose was 3.6 ± 0.4 mGycm, with an estimation of 1.8 mSv.

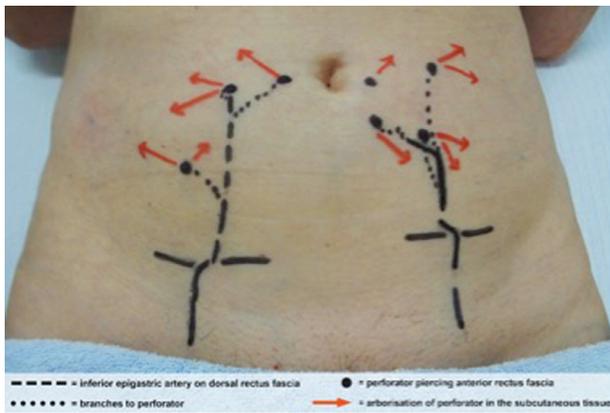


Fig. 2 Preoperative markings of CDU findings on the abdominal skin. Deep inferior epigastric artery is marked coming through posterior rectus fascia (horizontal line) and further course in cranial direction with its intramuscular branches and perforators. Subcutaneous arborization can help to plan the flap design.

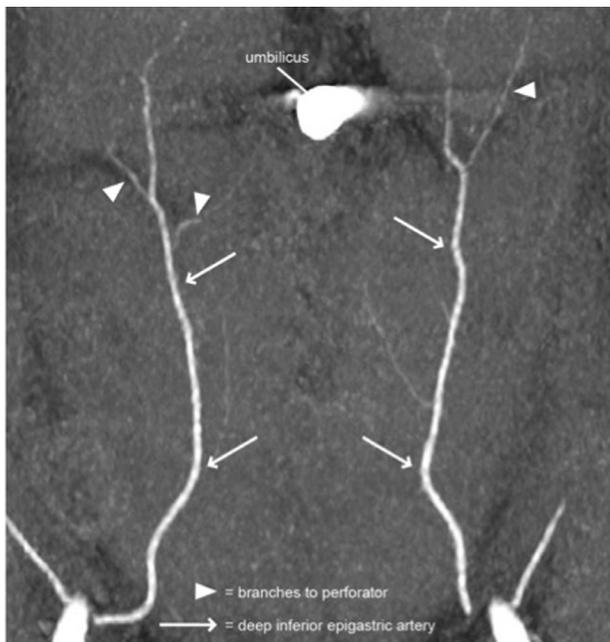


Fig. 3 Coronal CT section of the abdominal wall showing the inferior epigastric artery and its branches.

Subcutaneous and intramuscular course as well as the number and diameter of perforator vessels were visualized using the cardiovascular application of a commercially available post-processing software (syngo.via, Version 3.0, Siemens Medical Solutions, Forchheim, Germany) (Figures 3 and 4)

Procedure and documentation

CTA was performed one to seven days before surgery, and CDU usually one day before the procedure. Preoperative markings were applied by the leading surgeon the day before surgery and after the application of the CDU



Fig. 4 Axial CT section of the abdomen showing a perforator piercing the anterior rectus fascia.

markings in a standing position. The surgical team thoroughly examined both imaging entities preoperatively. All operations were carried out or supervised by one senior surgeon (MDH). Perforator configuration, size, number, intramuscular course and the decision-making process were precisely documented in operating reports. Postoperatively, all patients were monitored in the intermediate care unit for 24 h and usually released home by postoperative day 4-8. Outpatient visits were scheduled routinely at two and six weeks, and three, six, and twelve months after surgery. Wound healing, complications, adjuvant therapy, and quality of life were documented electronically at one, two, and six weeks and three, six, and twelve months after surgery. Data acquisition was performed retrospectively by previously routinely documented data. Written consent was obtained from all patients, the guidelines of the Declaration of Helsinki were followed throughout the study and the study was approved by the ethical committee.

Data collection

All breast reconstruction patients are routinely registered in our Breast Center database. We included patients who received a DIEP or a MSTRAM (muscle sparing Transverse Rectus Abdominis Muscle) flap autologous breast reconstruction between January 2015 and May 2017. All other microsurgical autologous breast reconstructions with, e.g., transverse myocutaneous gracilis (TMG), superior gluteal artery perforator (SGAP), or profunda artery perforator flap (PAP), were excluded. Only unipedicled flaps were included, bilateral DIEP flaps were calculated as one flap each.

When intraoperative clinical assessment showed no single sufficient perforator vein and/or artery decision to perform a MSTRAM flap was made. Patient characteristics such as age, BMI, comorbidities, history of smoking, BRCA

Table 1 Patient characteristics.

Patient characteristics, n = 98 (135 microsurgical breast reconstructions)	
Age in years, m (SD)	52.8 (10.9)
Body Mass Index in kg/m ² , m (SD; range)	25.9 (4.7; 18.6-42.2)
BRCA mutation carrier, n (%)	12 (12.2)
Smokers, n (%)	20 (20.4)
Diabetes mellitus, n (%)	7 (7)
Neoadjuvant therapy recipients, n (%)	36 (36.7)
Immediate reconstruction recipients, n (%)	66 (67)
↳ Nipple-sparing mastectomy, n (%)	34 (51.5)
↳ Skin-sparing mastectomy, n (%)	32 (48.5)
Bilateral reconstruction recipients, n (%)	26 (27)

mutation, and (neo) adjuvant therapy were assessed, along with intra- and postoperative complications and partial or total flap loss. Perforator identification, number, size (smaller or larger than 1 mm), and location in relation to the umbilicus were assessed, and correlated with CTA and CDU data and with intraoperative findings.

Statistical analysis

We report means (\pm SD/SEM) and medians (IQR). All statistical tests were performed at a significance level of $\alpha = 0.05$. The correlations were calculated using Pearson's correlation coefficient, and the odds were compared using a two-tailed Fisher's exact test. All analyses were performed using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego, CA, USA). The confidence level was set at 95%.

The manuscript was drafted following the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines.

Results

Between January 2015 and May 2017, 135 patients underwent microsurgical breast reconstruction at our institution, 125 of which were DIEP flap surgeries (in 98 patients). Patient characteristics are depicted in Table 1. The mean (SD) surgical time was 426 (123) minutes (range: 144-736) and the mean (SD) flap ischemia time was 75 (22) minutes (range: 37-167). The mean (SD) flap weight was 580 (280) g (range: 125 - 1750). One flap required intraoperative anastomosis revision (0.8%); and three flaps (2.4%) required revision operation within 72 h due to microsurgical compromise (venous thrombosis in two cases and arterial thrombosis in one case). Despite immediate revision, the venous thrombosis flap suffered complete and one of the arterial occlusion flaps suffered partial failure, both of which required further reconstructive surgery. Eleven hematomas occurred postoperatively (8.8%), five of which needed revision surgery (4%). Eleven breasts presented with mastectomy flap necrosis (8.8%), six of which required revision surgery; the remaining five healed with

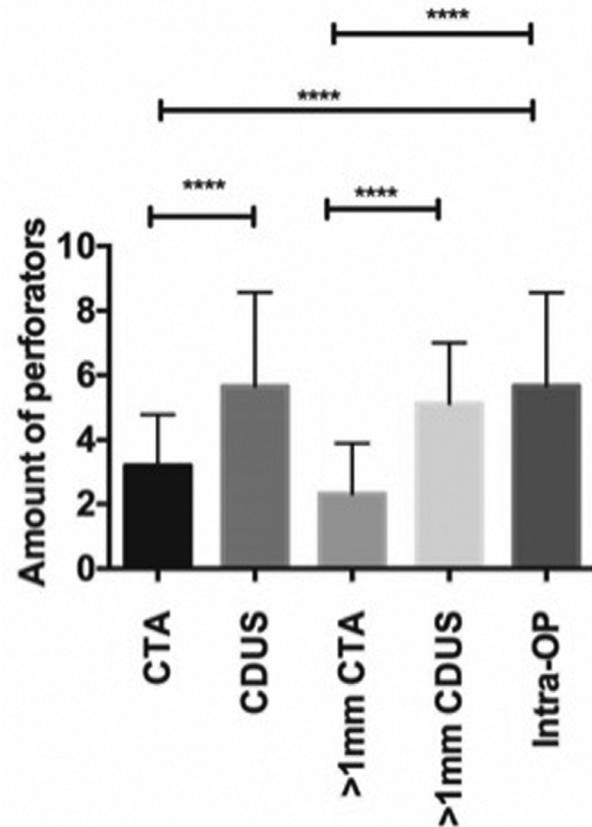


Fig. 5 Difference in the detection of number of perforators detected by CTA, CDU and intraoperatively. Column 1 + 2: average number of perforators detected by CTA and CDU Column 3 + 4: average number of perforators > 1 mm detected by CTA and CDU Column 5: average number of perforators detected intraoperatively **** = $p < 0.0001$.

conservative wound care only. Risk factor Analysis showed no significant impact on flap failure of any of the clinical factors (Smoking, BMI > 30, Age > 70 and Diabetes) Table 2.

Donor site complications were present in 17 patients (17.3%); seven (7.1%) of these were graded as major or IIIb according to the Clavien Dindo classification¹³ and 10 as minor or I-IIIa according to the Clavien Dindo classification. Specifically, seven patients developed a seroma (three of which needed revision surgery), nine showed delayed wound healing (four of which needed surgical intervention), and one case had a wound infection that was successfully treated with antibiotics.

Accuracy of CTA and CDU in perforator detection

The amount of perforators detected in CTA, CDU, and intraoperatively is shown in Figure 5. CTA readers documented mean (SD) 3.2 (1.5) perforators per patient (range 0-7), wherein mean (SD) 2.3 (1.6) were larger than 1 mm in size (range 0-6). CDU readers registered mean (SD) 5.6 (2.9) perforators per patient (range 0-12), wherein mean (SD) 5.1 (2.0) were larger than 1 mm in size (range 0-9). There were both significantly more perforators and more perforators

Table 2 Risk factor analysis.

Risk factors	OR (CI); NPV; PPV	p-value
Smoking (requiring recipient site revision)	0.9 (0.3-2.6); 0.8; 0.2	1
Smoking (requiring recipient site revision)	2.1 (0.6-7.9); 0.9; 0.1	0.26
BMI > 30 (requiring recipient site revision)	1.6 (0.5-4.9); 8.3; 0.2	0.50
Age > 70 years (requiring recipient site revision)	1.75 (0.2-16.7); 0.9; 0.2	0.50
Diabetes mellitus (requiring recipient site revision)	3.7 (1.0-13.5); 0.8; 0.5	0.05

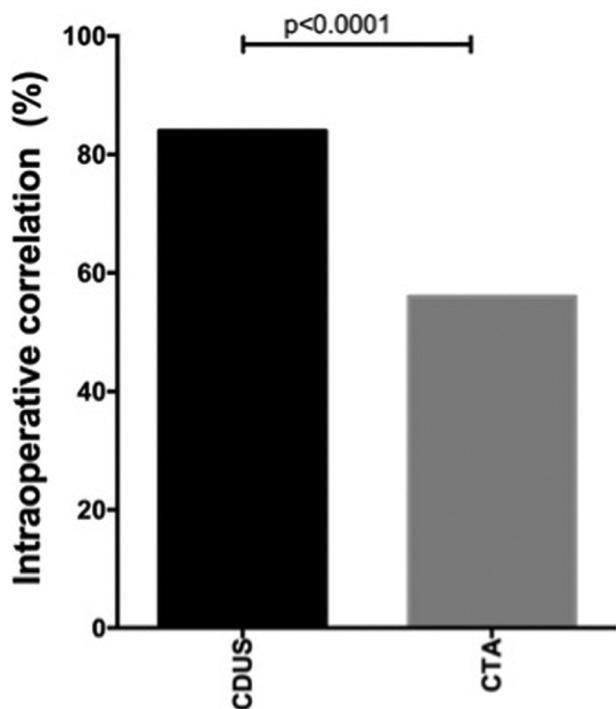


Fig. 6 Correlation of CDU and CTA with intraoperatively selected perforator(s). CTA ($r=0.01$, CI $-0.18-0.2$, $p=0.91$); CDU ($r=0.9987$, CI $0.9981-0.9991$, $p < 0.0001$).

larger than 1 mm in size in CDU than in CTA ($p < 0.0001$; [Figure 5](#)) **Decision making**

In 49 flaps (39.5%), one single perforator was chosen, and in 46 flaps (36.8%), a double perforator flap was performed. There was one case with intraflap anastomosis (0.8%). In seven cases, superficial inferior epigastric artery (SIEA) flaps were performed (5.6%). In 23 flaps (18.4%), more than two perforators were included and thus were counted as MSTRAM flaps. There was no significant correlation between the intraoperatively chosen perforator and the dominant perforators in the CTA ($r=0.01$, CI $-0.18-0.2$, $p=0.91$), whereas the correlation between the intraoperatively chosen perforator and the dominant perforators in CDU was significant ($r=0.9987$, CI $0.9981-0.9991$, $p < 0.0001$; [Figure 6](#)) However, this correlation had no influence on overall flap survival (positive predictive value of 0.9897 for CDU vs. 0.9836 for CTA). Moreover, we found a trend toward increased incidence of flap loss if neither CTA nor CDU correlated with the intraoperatively chosen perforator (Odds ratio = 4.483; CI 0.5068-39.65; $p=0.2171$).

Discussion

In our patient cohort, CDU showed significantly superior results concerning the accuracy of perforator selection and numbers of detected perforators than CTA. This is in contrast to what recent literature has suggested.

Until a decade after the first study by Blondeel et al. in 1998,¹⁴ CDU was widely thought to be an indispensable imaging tool for the planning of DIEP flap surgeries. In 2008, Rozen et al.¹⁵ have published the first prospective cohort study comparing CTA and CDU, which was even interrupted after eight patients due to superiority of CTA. Surprisingly, not a single perforator was detected with CDU in their study.¹⁵

Only few further studies have been published that directly compare CDU and CTA: Scott et al.¹⁶ have published a prospective study with 22 patients in 2010, which showed a 34% false negative rate in dominant perforator detection with CDU. On the other hand, Cina et al.⁵ have published a well-documented study in 2010 that demonstrated a 97% accuracy-rate of CDU and a 91% accuracy rate of CTA for dominant perforator detection, and a 90% accuracy rate of CDU and a 95% accuracy rate of CTA for perforator selection. CDU was superior to CTA in terms of perforator measurements, whereas CTA was superior to CDU for the estimation of the intramuscular course; considering X-ray exposure, the authors suggest to employ CTA only in selected cases.⁵

Several studies have demonstrated a reduction in the operating time since the introduction of CTA¹⁷ and a superiority of CTA over CDU for perforator number detection and outline of the intramuscular course,^{15,16} although some of those were performed with very small patient numbers. CDU, on the other hand, has lost its popularity in the last decade, and several studies confirmed CTA as the gold standard in preoperative DIEP imaging.^{16,18,19} O'Conner et al.¹⁷ compared the two years before the introduction of CTA at their institution with the time after its introduction and found shorter flap harvest times and as such reduced overall operating times, as well as a significant reduction of complications requiring a reoperation in the immediate postoperative period for the CTA as compared to the CDU. In contrast, the group of Klasson et al.²⁰ published data of a prospective randomized trial that compared CTA to handheld Doppler and found no statistical differences between the two groups concerning operating time and complication rate. Handheld doppler can rather be used as an adjunctive than a competitive modality compared to CDU and CTA, due to its inability to visualize, e.g., intramuscular perforator course. They conclude that improvement of operating time in DIEP flap breast reconstruction did not depend on the

used imaging tool, but rather on the experience gained over a period of time in the sense of a learning curve.²⁰

In our cohort, CDU detected significantly more perforators than CTA. Our data also revealed a stronger correlation between the dominant perforator in CDU and intraoperatively selected perforator than that for the CTA.

Because the avoidance of unnecessary X-ray exposure is of a very high priority for most radiology departments, one explanation for these findings might be our routinely used dose adapted CTA protocol, with only 1.8-2.9 mSv (compared to 10 mSv of a conventional CT abdomen). As a consequence, less perforators might be detected, especially perforators smaller than 1 mm. For an inexperienced eye, quality of this dose-adapted CTA might seem inferior than a high-dose CTA. However, the group of Niumsawatt et al.²¹ demonstrated that with adaptive statistical iterative reconstruction (ASiR) technology, a radiation reduction of 60% is possible without compromising the image quality. For the preoperative planning, the number of detected perforators as such is of less significance, as dominant perforators, bifurcation type, and luminal diameters play a more important role. Nonetheless, smaller perforators may still be important, depending on their position, when the surgeon chooses to include more than one perforator into the flap design.

Another explanation for our demonstrated superiority of the CDU over the CTA might be that only highly specialized angiologists performed the CDUs for our breast center patients. Interobserver variability has otherwise been a constant hurdle when comparing CDU with the more observer-independent CTA.⁶ The often discussed inter-observer variability as a drawback of CDU might though lose some of its relevance, as modern microsurgical breast reconstruction is usually offered by high volume centers, where interdisciplinary specialists are well experienced. In fact, recent studies could already prove that increasing numbers of microsurgical breast reconstructions and the creation of breast centers with specialized teams of every discipline strongly improves the quality of treatment.²² Another argument favoring radiation free imaging tools are the rising numbers of prophylactic mastectomies and reconstruction in BRCA carriers, with consequently a significantly younger patients group in the cohort of mastectomy candidates.²³

MRA has recently been proposed as an alternative nonionizing tool with promising results.^{8,24} Compared to CTA though, MRA is an expensive and lengthy procedure with potential artefacts as a drawback in the imaging reconstruction.⁹

We found an overall complication rate of 10.4% at the recipient site and 7% at the donor site that required revision in our patients, and one total flap loss due to venous occlusion and one partial flap loss due to arterial occlusion. A recent review of Knox et al.⁴ on 138 DIEP flaps reported comparable complication rates.

An interesting finding of our study, although not statistically significant because of low incidence of this major complication, was a trend toward partial and total flap loss in cases where neither CDU nor CTA correlated with the intraoperatively chosen perforator. In the case that resulted in total flap loss, an SIEA flap had been performed. This decision was made intraoperatively by the senior surgeon. Flap loss occurred following venous thrombosis and

unsuccessful revision surgery. In the other case, because of partial flap necrosis following revision surgery, the lead surgeon had intraoperatively chosen a different perforator than the one suggested as dominant by CDU and CTA.

This finding emphasizes the importance of preoperative imaging in DIEP flap breast reconstruction, and it somewhat justifies the implementation of both imaging studies that is standard at our institution, even if this can be associated with higher total costs. However, our billing of most cases occurs on a cost per diagnosis basis. Therefore, the costs for the patients are not increased by additional imaging studies.

A novel argument that supports CTA in the preoperative planning of DIEP surgery is the obtainment of valuable additional information, which can be obtained by morphometric measurements, e.g., a patient's individual risk of donor site complications following abdominally based microsurgical breast reconstruction.^{25,26}

Our study has several limitations: First, we used a retrospective study design. As a consequence, our study did not have a control group, which represents a major drawback. Furthermore, surgical planning is finalized after CDU markings have been completed. The latter could potentially influence the lead surgeon in his or her pre- and intraoperative decision-making more strongly than the CTA images on a computer screen do. We strongly believe that additional prospective randomized trials are needed to validate our results.

Conclusions

CDU as performed by experienced hands is a reliable diagnostic tool in the preoperative work up of DIEP flap microsurgical breast reconstructions, without the risk and potential consequences of X-ray exposure. CTA continues to be an important tool and might even gain more importance in the future, as more and more additional variables can be obtained by its usage.^{25,26} Any conclusion for clinical practice should first be confirmed by prospective randomized controlled trials that re-evaluate our preliminary results. However, our results emphasize the importance of preoperative imaging tools as part of the gold standard in DIEP flap breast reconstruction.

Declaration of Competing Interest

None.

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Supplementary material

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2019.06.008.

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