



“NACsomes”: A new classification system of the blood supply to the nipple areola complex (NAC) based on diagnostic breast MRI exams[☆]

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Received 12 August 2014; accepted 9 February 2015

KEYWORDS

Breast;
Magnetic resonance
imaging;
Nipple-areola
complex;
Oncoplastic

Summary *Background:* Breast MRIs have become increasingly common in breast cancer work-up. Previously obtained breast MRIs may facilitate oncoplastic surgery by delineating the blood supply to the nipple-areola complex (NAC). The aim of this study was to identify and classify the *in vivo* blood supply to the NAC using breast MRI exams.

Methods: Breast MRIs obtained over a one-year period were retrospectively reviewed. Patients with negative MRI findings (BI-RADS category 1) were included; patients with diagnoses of breast cancer or previous breast surgery were excluded. Twenty-six patients were evaluated. Dominant blood supply was determined by maximum filling at 70 s post-contrast. Blood supply to the NAC was classified into five anatomic zones: medial (type I), lateral (type II), central (type III), inferior (type IV) and superior (type V).

Abbreviations: BCT, breast conservation therapy; BI-RADS, breast imaging-reporting and data system; CTA, computed tomographic angiography; DIEP, deep inferior epigastric perforator; ICG, indocyanine green; MIP, maximum intensity projection; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; NAC, nipple-areola complex.

[☆] Part of the work has been presented at Plastic Surgery 2010, 79th annual scientific meeting of the American Society of Plastic Surgeons (ASPS), Oct. 1–5, Toronto, Canada, at the 16th International Congress of the International Confederation for Plastic Reconstructive and Aesthetic Surgery (IPRAS), May 22–27, 2011, Vancouver, Canada, and the World Society of Reconstructive Microsurgery 6th Congress, June 29–July 2, 2011, Helsinki, Finland. The abstract of above listed presentations has been published in Plastic & Reconstructive Surgery. 126(suppl):27, October 2010 and in the Can J Plast Surg 2011, Vol 19 Suppl A Summer: 44–45.

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<http://dx.doi.org/10.1016/j.bjps.2015.02.027>

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Results: Patient age ranged from 33 to 70 years. Fifty-two breasts were evaluated and 80 source vessels were identified (37 right, 43 left). Twenty-eight breasts had type I only blood supply, 22 breasts had multi-zone blood supply (type I + II, $n = 20$; type I + III $n = 2$), one breast had type II only blood supply, and a single breast had type III only blood supply. Anatomic symmetry was observed in 96% of patients.

Conclusion: This study utilized MRI to evaluate *in vivo* vascular anatomy of the NAC, classify NAC perfusion ("NACsomes"), and assess vascular symmetry between breasts. Superomedial source vessels supplying the NAC were predominant. Preoperatively defining NAC blood supply may aid planning for oncoplastic procedures.

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Introduction

Approximately one of every eight women in the United States will develop breast cancer during her life.¹ With early detection, improved adjuvant therapy, and better understanding of tumor biology, more women are opting for breast conserving therapy (BCT). Long-term follow-up studies have demonstrated no significant difference in disease-free survival, relapse-free survival, or overall survival comparing total mastectomy and BCT.^{2,3} As such, the field of oncoplastic surgery, combining the tenets of oncologic surgery and reconstructive plastic surgery, has become increasingly popular. Ideally, oncoplastic surgery provides aesthetically pleasing results, while achieving appropriate oncologic margins.⁴⁻⁶ However, one potential pitfall of the oncoplastic approach is the uncertainty of the blood supply to the nipple-areola complex (NAC). When utilizing an oncoplastic approach, it is important to consider perfusion to the NAC prior to choosing the vascular pedicle upon which to relocate the NAC. Pre-operative imaging may be helpful in this planning process.

The blood supply to the NAC has been defined in various cadaver studies⁷⁻⁹ and seems to originate from several sources, including the internal thoracic artery (internal mammary artery), lateral thoracic artery (external mammary artery), thoracoacromial artery, superior thoracic artery (highest thoracic artery), or anterior/posterior branches of the intercostal arteries. Dominant blood supply to the NAC appears to be attributable to the internal thoracic artery and/or the lateral thoracic artery in the vast majority of these studies.⁷⁻⁹ However, there is a paucity of data correlating these anatomic findings with *in vivo* perfusion studies of the NAC.

The role of *in vivo* imaging techniques evaluating tissue perfusion patterns and perforator anatomy (angiosomes) preoperatively has increased in microsurgical breast reconstruction over the past several years. Computed tomographic angiography (CTA) represents the gold standard in preoperative vascular perforator imaging, and preoperative CTA for deep inferior epigastric perforator (DIEP) evaluation has become common practice in many institutions.¹⁰⁻¹² Dependent on the specific anatomic location, disease and tissues to evaluate, magnetic resonance angiography (MRA) maintains or enhances the imaging quality without ionizing radiation.^{13,14} This advantage

combined with a very high sensitivity has led to increased use of MRI based imaging in the workup of many diseases.

MRI for breast cancer diagnosis and workup was initially used as a second line modality in selected clinical scenarios such as equivocal mammographic and/or ultrasound findings. Currently, MRI is used not only as an adjunct, but also as a first line modality for screening in selected subsets of women with an increased lifetime risk for breast cancer.^{15,16} Although the sensitivity for breast MRI is quite high, its lack of specificity has limited its use as a general screening method for the detection of breast cancer.¹⁷ Regardless of the ongoing debate concerning breast MRI indications, the use of breast MRI has increased 20-fold since 2000.¹⁸ The increased use of MRI for both screening and pre-operative tumor evaluation could offer a potential benefit in delineating the *in vivo* blood supply to the NAC, and this information could be used for pre-operative surgical planning in oncoplastic and reconstructive procedures. Previously obtained diagnostic imaging may negate the need for additional angiographic studies.¹⁹

The aim of this study is to identify and classify the blood supply to the NAC ("NACsomes") using early phase MRI images from patients undergoing MRI for clinical evaluation. An attempt is made to compare *in vivo* NAC perfusion via MRI with cadaver NAC perfusion studies. To the authors' knowledge, this is the first study evaluating specific *in vivo* arterial perfusion to the NAC, and the largest study specifically addressing NAC perfusion.

Patients and methods

Following IRB approval, bilateral breast MRIs of 26 female patients, obtained over a one-year period, were retrospectively reviewed by the breast MR radiologist (SF). Inclusion criteria were breast MRIs with a Breast Imaging-Reporting and Data System (BI-RADS) category 1 assessment (negative examination). Patients with a known diagnosis of breast cancer or previous breast surgery were excluded, while those with prior core biopsies were eligible. The reviewed indications for breast MRI included at least one of the following: breast nodule or cyst ($n = 12$), abnormal mammogram and/or ultrasound ($n = 7$), screening due to a strong family history of breast cancer ($n = 6$), dense or painful breasts ($n = 5$), or history of ovarian cancer ($n = 1$) (Table 1).

Table 1 Indication for Breast MRI.

Reason for breast MRI	Number of patients
Breast nodule or cyst	12
Abnormal mammogram	7
Strong family history of breast cancer	6
Dense, painful breasts	5
History of ovarian cancer	1
Patients had one or more of the above reasons listed to undergo MRI of the breasts.	

Bilateral breast MRIs were performed using an MRI scanner (Siemens 1.5T MAGNETOM Espree, Sentinelle 8 Channel Breast Coil, Munich, Germany). Pre-contrast images were obtained, followed by post-contrast (Magnevist, gadolinium) images at 70-s after a 20-s delay. (Table 2: Protocol) Axial, coronal and sagittal images were evaluated in addition to maximum intensity projection (MIP) images (Figure 1). The determination of the dominant blood supply was based upon the timing of contrast filling (maximum fill at 90 s).

Blood supply to the NAC was classified into 5 anatomic zones ("NACsomes"): medial (type I), lateral (type II), central (type III), inferior (type IV) and superior (type V). Further sub-classification was performed based upon the source vessel for medial and lateral zones (types I and II)—medial (type I) blood supply (a) superomedial, (b) medial, (c) inferomedial; lateral (type II) blood supply, (a) superolateral, (b) lateral (c) inferolateral (Figure 2).

Results

All 26 patients were female, and images of 52 breasts were reviewed. Patient age ranged from 33 to 70 years (mean 49 years, median 45.5 years). The total number of source vessels to the NAC identified on MRI was 80 (right breast = 37, left breast = 43). Assessment of the 52 breast MRI images revealed that 28 breasts had type I only blood

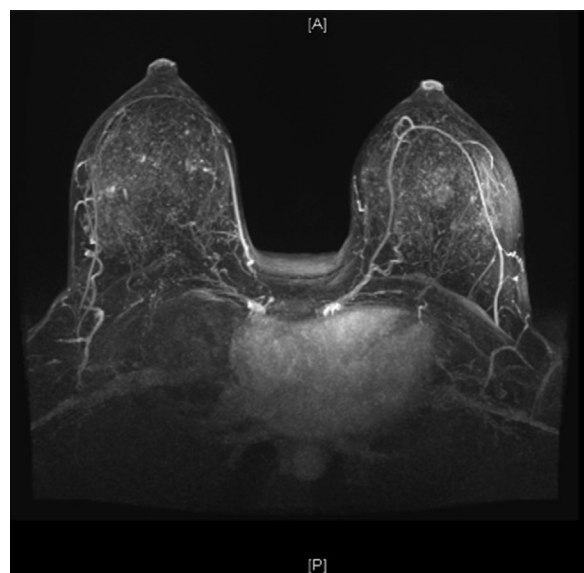


Figure 1 Single cut of a representative MRI (MIP) image of both breasts. This patient has a multi-zone blood supply to the NAC, which was classified as Type Ib, IIa, III on the left and Type Ib, IIa on the right, based on multiple cuts of the MRI images including MIPs, coronal, axial and sagittal.

supply (53.9%), one breast had type II only (1.92%), and another breast a type III only (1.92%) blood supply. Twenty-two breasts (42.30%) had multi-zone blood supply type I with II, $n = 20$ (38.46%); type I with III, $n = 2$ (3.84%), Table 3.

Right breast

Evaluation of the right breast indicated that 16 patients had medial zone (type I) only blood supply, two of which had an additional medial zone vessel. A single patient had lateral zone only blood supply (type II), and nine patients had multi-zone blood supplies. Of the nine patients with multiple zone blood supplies, eight were medial and lateral

Table 2 Parameters of breast MRI protocol for diagnostic workup of breast disease.

Parameters	1	2	3	4	5	6	7
Sequence	SCOUT	COR STIR	AX T2 TSE BILAT	AX T1 NON FS	AX T1 SPAIR TEST-1.4	AX T1 DYNAMIC SPAIR-1.4	AX T1 3D-1.2
Thickness (mm)		4	4	1.4	2	2	1.6
Gap (mm)		1	1	0	0	0	0
Scan matrix		256 × 256	358 × 512	307 × 384	346 × 384	346 × 384	426 × 448
N _{ex}		1	1	1	1	1	1
Flip angle (°)		180	25	25	10	10	10
Phase		RL	RL	RL	RL	RL	RL
Frequency		HF	AP	AP	AP	AP	AP
TR		6300	4000	8	4.56	4.56	5.36
TE		61	102	4.5	2.13	2.13	2.49
Acquisition (t)		5 m 41 s	4 m	3 m 16 s	1 m 29 s	1 m 29 s	2 m 56 s

COR = coronal; STIR = short T1-inversion recovery; AX = axial; TSE = turbo spin echo; FS = fat suppressed; SPAIR = spectral adiabatic inversion recovery; HF = head to foot, also referred to as superior-inferior (SI); Nex = number of excitations; TR = The repetition time; TE = Echo delay time or time to echo.

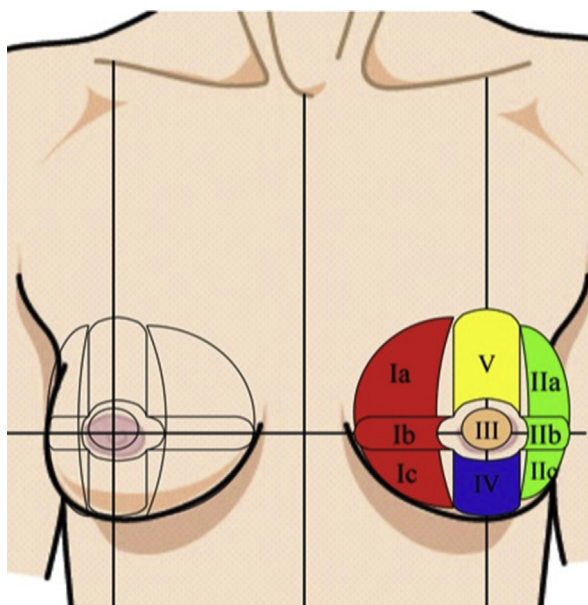


Figure 2 Schematic image of the breast with classification of source vessels supplying the NAC. Type I red, Type II green, Type III beige, Type IV blue, Type V yellow.

sources (types I and II), and one had medial and central source vessels (types I and III). Analyzing the eight patients with both medial and lateral perfusion, four patients had equal medial and lateral dominant supply, two patients had

lateral predominant perfusion, and two had medial dominant supply. A total of 25 out of 26 right breasts (96%) had NAC perfusion derived from a medial source vessel; 11 out of 26 breasts (42.3%) had more than one vessel supplying the NAC. More detailed vessel distribution can be seen in [Tables 4 and 5](#), and [Figure 3](#).

Blood vessel diameter on the right breast ranged from 1 to 6 mm for the dominant vessels, and 2–3 mm for secondary blood supply. When a single vessel was present ($n = 15$ patients) the average diameter was 2.5 mm, and when two vessels were present ($n = 11$ patients) the average diameter was 2.89 mm.

Left breast

Evaluation of the left breast indicated that 12 patients had medial zone only blood supply (type I), 13 patients had multi-zone blood supply, and one patient had a central zone only blood supply (Type III). Two of the patients with medial zone only vessels had two additional medially derived vessels. Of the 13 patients with multiple zone blood supplies, the medial source vessel was present in all patients; 12 patients had an additional lateral source (types I and II), and one patient had an additional central perforator (types I and III). There were two breasts with three vessels supplying the NAC. Evaluating dominance in the 12 patients with both medially and laterally derived vessels (including the two breasts with three vessels), 3 out of 12 patients had equal medial and lateral dominant supply, 8

Table 3 NAC perfusion types and percent per breast.

Classification (per breast, $n = 52$)	Total breasts ($n = 52$) (%)	Right breast ($n = 26$) (%)	Left breast ($n = 26$) (%)
Type I (medial) only	28 (53.9%)	16 (61.54%)	12 (46.15%)
Type II (lateral) only	1 (1.92%)	1 (3.85%)	0 (0%)
Type III (central) only	1 (1.92%)	0 (0%)	1 (3.85%)
Type IV (inferior) only	0 (0%)	0 (0%)	0 (0%)
Type V (superior) only	0 (0%)	0 (0%)	0 (0%)
Multiple zone blood supply	22 (43.3%)	9 (34.62%)	13 (50%)
Type I and II	20 (38.46%)	8 (30.77%)	12 (46.15%)
Type I and III	2 (3.84%)	1 (3.85%)	1 (3.85%)

Table 4 Classification and distribution of 80 source vessels supplying the NAC of 52 breasts.

Classification type (vessel source)		Number of vessels identified ($n = 80$)		
		Right breast ($n = 37$)	Left breast ($n = 43$)	Total n and % of each type
Type I (medial)		27	28	55 (68.75%)
Subtype	Ia-superomedial	19	18	37
	Ib-medial	6	7	13
	Ic-inferomedial	2	3	5
Type II (lateral)		9	12	21 (26.25%)
Subtype	IIa-superolateral	6	6	12
	IIb-lateral	3	4	7
	IIc-inferolateral	0	2	2
Type III (central)		1	3	4 (5%)
Type IV (inferior)		0	0	0
Type V (superior)		0	0	0

Table 5 Distribution of 80 source vessels supplying the NAC in each breast, by percent.

Classification (number of source vessels for NAC perfusion, n = 80)	Right breast (n = 37)	Left breast (n = 43)
Type I (medial)	73.0%	65.1%
Subtype Ia-superomedial	51.3%	41.9%
Ib-medial	16.2%	16.3%
Ic-inferomedial	5.4%	7.0%
Type II (lateral)	24.3%	28.0%
Subtype IIa-superolateral	16.2%	13.9%
IIb-lateral	8.1%	9.3%
IIc-inferolateral	0%	4.6%
Type III (central)	2.7%	7.0%
Type IV (inferior)	0%	0%
Type V (superior)	0%	0%

out of 12 patients had medially derived dominant vessels, and only one out of 12 had laterally dominant vessels. A total of 25 out of 26 left breasts (96%) had NAC perfusion derived from medial source vessels; 15 out of 26 breasts (57.7%) had more than one vessel supplying the NAC. More detailed vessel distribution can be seen in [Tables 3 and 4](#), and [Figure 3](#).

Blood vessel diameter ranged from 1 to 5 mm for the dominant vessels and 2–4 mm for the secondary supply. When a single vessel was present (n = 11 patients) the average diameter was 2.36 mm, when two vessels were present (n = 13 patients) the average diameter was 2.73 mm, and when three vessels were present (n = 2 patients) the average diameter was 2.33 mm.

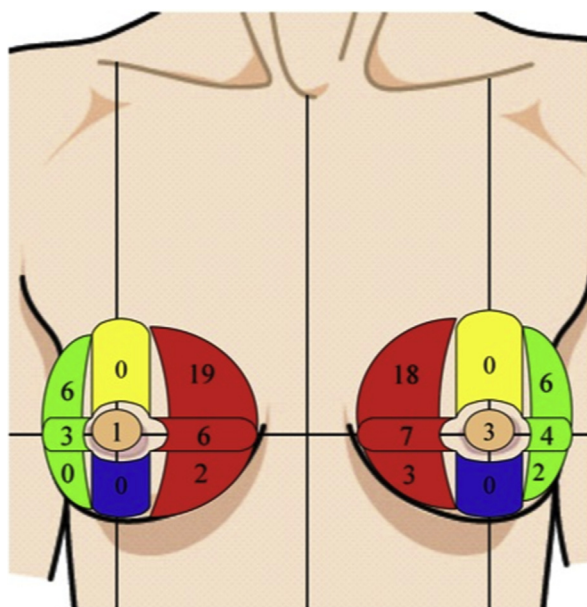


Figure 3 Schematic image of the breast with classification and distribution of source vessels supplying the NAC. N = 80 source vessels identified in 52 breasts, 37 vessels on the right, and 43 vessels on the left. Type I red, Type II green, Type III beige, Type IV blue, Type V yellow.

Evaluation of symmetry

Comparison of the right and left breast demonstrated similar anatomic distributions in 96% of patients. Of these patients, 52% had identical perfusion zones, while 48% had an additional zone of blood supply in one breast. Only a single patient (4%) had completely different perfusion zones in each breast.

Discussion

NAC perfusion has been studied in cadavers and/or descriptions of reduction mammoplasty techniques. Cunningham, the first to review contemporary literature on breast vasculature, noted the main vasculature supply to the breast was from the lateral mammary artery and the internal thoracic (mammary) artery—branches which form a plexus in the anterior fat layer.²⁰ Subsequently, NAC perfusion was specifically addressed in a technical description of reduction mammoplasties using a central, glandular breast pedicle. This pedicle was based on contributions from the lateral thoracic artery, intercostal perforators, internal thoracic (mammary) artery, and the thoracoacromial artery.²¹ An anatomic study of arteries related to NAC perfusion was reported by Nakajima et al. using five fresh cadavers and radiographic imaging; they concluded that the dominant blood supply to the NAC was from branches of the external and internal mammary arteries that communicate above and below the areola.⁸

More recent studies have helped delineate perfusion to the NAC. Wuringer et al. described a fibrous connective tissue septum running horizontally from the pectoral fascia along the fifth rib towards the nipple.²² They corroborated previous studies of blood supply to the NAC and concluded that the main supplying vessels along the fibrous septum were the thoracoacromial artery, intercostal arteries, and the internal and lateral thoracic arteries. Upon methylene blue filling, they found that the internal thoracic artery perfused the NAC more intensely via perforating branches from anastomoses with the intercostal arteries. The original findings reported by Wuringer have been studied further, and provide the basis of some reduction mammoplasty techniques.^{23,24}

Two eloquent cadaver dissections reported the arterial vasculature of the NAC, after intra-arterial injections, and different dissection techniques. Van Deventer et al. dissected 27 female breasts after intra-arterial latex injections and found that the NAC was perfused by the internal thoracic artery (48.8%), its perforating branches and the anterior intercostal arteries (24.4%), and the lateral thoracic artery (23.2%).⁷ All of the breasts evaluated had at least one vessel from the internal thoracic (mammary) artery supplying the NAC, and the authors suggest that this artery is the main, most reliable source of NAC perfusion. Further description of NAC vascular anatomy described numerous anastomoses, with most anastomoses (50%) occurring between the internal thoracic and lateral thoracic arteries. In a smaller study using microdissection, O'Dey et al. found that the lateral thoracic artery was the most reliable NAC-supporting artery.⁹ The major arteries supplying the NAC were the lateral thoracic artery, internal

mammary artery, anterior branches of the intercostal arteries, and the highest thoracic artery (descending reproducibility). Branches from the lateral thoracic artery to the NAC were found in all 14 breasts (100%), and perforators from the internal mammary artery supplying the NAC were found in 86%. O'Dey et al. based their study on evaluating various NAC-bearing pedicles, and also employed a classification scheme of four zones.

The majority of previous studies has been limited to analyses of cadaver specimens and thus may not reflect physiologic perfusion of the NAC. The advantage of this study is the assessment of NAC vascular supply in live human subjects undergoing contrast breast MRI for other diagnostic purposes. Our results, based on the arterial filling phase of contrast breast MRIs describe NAC perfusion zones "NACsomes." The distribution of "NACsomes" suggest that medial source vessels ("NACsome" type I) provide the most reliable perfusion source to the NAC- specifically superomedial originating vessels. This is most consistent with the findings of Van Deventer et al., rather than O'Dey et al. (see Table 6 for comparison of NAC perfusion studies). The difference is most likely attributable to different methodologies, but there is interplay and anastomoses between major NAC-perfusing vessels. Just as Van Deventer et al. noted the numerous anastomoses between the internal thoracic artery and lateral thoracic artery, we found that in those breasts whose NAC was perfused by multiple zones, it was usually an interplay between medial and lateral zones.

The majority of previous studies, have focused on arterial perfusion of the NAC, but it is important to note the implications of venous drainage; LeRoux et al. studied venous drainage of the NAC in 16 cadaver breasts and reported that the NAC is drained by a superficial subareolar

ring of veins that drain medially (to internal mammary vein) and laterally (to lateral thoracic and subclavian veins).²⁵ They note that medial veins tend to be more superficial, while lateral veins are deeper, and conclude that medial and inferior pedicles contain the most extensive and consistent venous outflow. Our study, much like previous studies, has focused on arterial perfusion but it is critical to remember the relationship of arterial supply with its venous return. Although less common, venous congestion may be associated with specific NAC-related wound healing complications.

Our study utilized previously obtained diagnostic MRI images, not originally intended for preoperative planning. Breast MRI is highly sensitive, but its use in breast screening has been limited by its cost, low specificity, and invasiveness (contrast). Although breast MRI as a screening tool continues to be debated, its use over the last decade has increased 20 fold; the increase in breast MRIs was for all indications, but particularly for screening and surveillance.¹⁸ Screening is only recommended as an adjunct for those patients with a greater than 20% lifetime risk, secondary to genetics and strong family history.²⁶ However, diagnostic indications have significantly contributed to the number of patients who have been evaluated with MR. The most common indication for breast MRIs of patients included in our study was for breast nodules or cysts, followed by abnormal mammogram, and strong family history of breast cancer (Table 1). Regardless of the debate over indications for breast MRIs the likelihood that a patient has been imaged with this modality is increasing.

We believe that breast MRI exams provide valuable information in assessing vascular anatomy of the NAC. This includes the arterial filling phase, venous drainage phase and 3D reconstructed MIP images. Reviewing these images

Table 6 Review of studies specifically evaluating perfusion to the nipple areola complex (NAC).

Study	Methods	n	Conclusions
Nakajima 1995	Radiographically Lead Oxide Injection Cadaver	5 Cadavers	<ul style="list-style-type: none"> - Branches of external and internal mammary arteries are dominant blood supply to NAC. - Only a subcutaneous pedicle medially or laterally will provide adequate blood supply to the NAC.
Van Deventer 2004	Anatomical Dissection Latex Injection Cadaver	27 Breasts	<ul style="list-style-type: none"> - Internal thoracic arteries are the main, and most reliable source of NAC perfusion. - 27/27 internal thoracic artery. - 20/27 anterior intercostal arteries. - 19/27 lateral thoracic artery.
O'Dey 2007	Microdissection Lead Oxide Injection Cadaver	7 Cadavers	<ul style="list-style-type: none"> - Perforators from internal mammary artery 86% - Anterior branches of intercostal arteries 71% - Highest thoracic artery 57% - Lateral thoracic artery 100%
Seitz <i>Present Study</i>	Magnetic Resonance Gadolinium Contrast In Vivo Patients	52 Breasts	<ul style="list-style-type: none"> - Superomedial source vessels (internal mammary artery) were predominate NAC perfusion. - 50/52 medial source vessel (internal mammary artery) - 21/52 lateral source vessel (lateral thoracic artery) - 3/52 central source vessel

in a multidisciplinary approach, such as institutional breast conferences, can be helpful. In our study group we did not find any source vessel to the NAC originating in the inferior quadrant (type IV). An infero-lateral source vessel (type IIc) was only found as a secondary blood supply to the NAC in 2 out of 80 vessels. The reduced risk of NAC necrosis with an infero-lateral infra-mammary-fold (IMF) incision rather than a peri-areola incision for nipple sparing mastectomy (NSM) as reported by Colwell et al. could be related to preservation of the dermal and sub-dermal NAC perfusion and furthermore choosing an incision away from substantial NAC source vessels.²⁷ Pre-operative communication between the reconstructive and oncologic surgeon, as to incision choice and perforator preservation based on their breast MRI exam, may lead to improved results with a decrease in wound healing complications.

Intraoperative assessment of tissue perfusion can be done with the help of indocyanine green (ICG) fluorescence angiography. This is a helpful modality in assessment of mastectomy flap perfusion, flap perfusion in general, and NAC perfusion.^{28,29} This technique mainly serves as an intraoperative tool, rather than a preoperative tool. Reviewing previously obtained diagnostic breast MRIs prior to the planned procedure may reduce the need for intraoperative ICG fluorescence angiography to evaluate NAC perfusion.

A study evaluating previously performed diagnostic exams, and their usefulness for microsurgical-reconstruction and preoperative planning, concluded that often there is sufficient information rendering additional angiographic studies unnecessary.¹⁹ Schellekens et al. evaluated internal mammary perforators, and found that 11 out of 12 previously obtained MRIs provided sufficient information regarding the dominant perforators. Interestingly, perforator dominance differed from previous cadaver studies.¹⁹ Although patients included in our study were non-operative cases, we feel that previously obtained images would be sufficient for preoperative planning; this parallels the aforementioned study.

To our knowledge, this is the first *in vivo* study specifically addressing the arterial vascular supply to the NAC and establishing a classification system of "NACsomes". Other studies have examined NAC and skin flap perfusion intraoperatively, but without identification of specific vessels.²⁹ Intraoperative NAC perfusion can be evaluated with ICG fluorescence angiography, and Wapnir et al. employed this method to classify NAC perfusion originating from underlying breast tissue (18%), surrounding skin (46%), or a combination of both (36%).²⁹ Although our classification differs significantly, we found it useful to classify vasculature based on zones of vessel origin—similar to a classification scheme developed by O'Dey et al.⁹

Our study is limited by the fact that, although it is an *in vivo* model, there may be non-physiologic flow parameters based on the prone position and distortion of breast volumes during breast MRI. Additionally, we did not correlate blood supply with breast volume. This study, however, has clinically advantageous components because a significant number of women have breast MRIs available from previous diagnostic workups. This can provide the oncologic and plastic surgeon with sufficient information for collaborate preoperative planning.

Conclusion

Previously obtained breast MRIs may be helpful in defining NAC blood supply. This information can be evaluated preoperatively, and can be used for reconstruction/oncoplastic surgery, or reduction mammoplasties. These vessels can be classified into anatomical zones "NACsomes". The main source vessel for the NAC is superomedial, and NAC blood supply is symmetric. Perfusion to the NAC during *in vivo* MRIs compares to vasculature determined by cadaver studies.

Ethical approval

This study was approved by the Institutional Review Board.

Funding

None.

Conflict of interest statement

The authors have no conflicts of interests and no financial disclosures. Data was gathered in accordance with the institutional review board.

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