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CLINICAL INVESTIGATION

Tumor Contact With Internal Mammary Perforator Vessels as Risk Factor for Gross Internal Mammary Lymph Node Involvement in Patients With Breast Cancer

Sophie T. Behzadi, MD,* Rebecca Moser, MD,* Sophia Kiesl, MD,* Jana Nano, PhD,* Jan C. Peeken, MD,* Julius C. Fischer, MD,* Eva M. Fallenberg, MD,† Thomas Huber, MD,† Bernhard Haller, PhD,‡ Evelyn Klein, MD,§ Marion Kiechle, MD,§ Stephanie E. Combs, MD,*,‖,¶ and Kai J. Borm, MD*

*Department of Radiation Oncology, TUM School of Medicine and Health, Technical University Munich (TUM), Klinikum rechts der Isar, Munich, Germany; †Department of Radiology, TUM School of Medicine and Health, Technical University Munich (TUM), Klinikum rechts der Isar, Munich, Germany; ‡Institute of AI and Informatics in Medicine, TUM School of Medicine and Health, Technical University Munich (TUM), Klinikum rechts der Isar, Munich, Germany; §Department of Gynecology and Obstetrics, TUM School of Medicine and Health, Technical University Munich (TUM), Klinikum rechts der Isar, Munich, Germany; ‖Deutsches Konsortium für translationale Krebsforschung (DKTK) — Partner Site Munich, Munich, Germany; and ¶Institute of Radiation Medicine, Helmholtz Zentrum München, Munich, Germany

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Purpose: The identification of internal mammary lymph node metastases and the assessment of associated risk factors are crucial for adjuvant regional lymph node irradiation in patients with breast cancer. The current study aims to investigate whether tumor contact with internal mammary perforator vessels is associated with gross internal mammary lymph node involvement.
Methods and Materials: We included 297 patients with primary breast cancer and gross internal mammary (IMN+) and/or axillary metastases as well as 230 patients without lymph node metastases. Based on pretreatment dynamic contrast-enhanced magnetic resonance imaging, we assessed contact of the tumor with the internal mammary perforating vessels (IMPV).
Results: A total of 59 patients had ipsilateral IMN+ (iIMN+), 10 patients had contralateral IMN+ (cIMN+), and 228 patients had ipsilateral axillary metastases without IMN; 230 patients had node-negative breast cancer. In patients with iIMN+, 100% of tumors had contact with ipsilateral IMPV, with 94.9% (n = 56) classified as major contact. In iIMN− patients, major IMPV contact was observed in only 25.3% (n = 116), and 36.2% (n = 166) had no IMPV contact at all. Receiver operating characteristic analysis revealed that "major IMPV contact" was more accurate in predicting iIMN+ (area under the curve, 0.85) compared with a multivariate model combining grade of differentiation, tumor site, size, and molecular subtype (area under the curve, 0.65). Strikingly, among patients with cIMN+, 100% of tumors had contact with a crossing contralateral IMPV, whereas in cIMN− patients, IMPVs to the contralateral side were observed in only 53.4% (iIMN+) and 24.8% (iIMN−), respectively.
Conclusions: Tumor contact with the IMPV is highly associated with risk of gross IMN involvement. Further studies are warranted to investigate whether this identified risk factor is also associated with microscopic IMN involvement and whether it can assist in the selection of patients with breast cancer for irradiation of the internal mammary lymph nodes.

Corresponding author: Kai J. Borm, MD; E-mail: kai.borm@mri.tum.de
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Introduction

Depending on the tumor site, 10% to 52% of primary tumors in breast cancer show primary lymphatic drainage to the internal mammary lymph nodes (IMN).[1] Older surgical studies found gross internal mammary involvement in up to 30% of patients with positive axillary nodes.[2] Even though IMN biopsy can be incorporated into reconstruction practices,[3] surgical resection of IMN is not a standard procedure today. The diagnosis of IMN with imaging, on the other hand, is challenging as the criteria and methodology for detection of IMN metastases are controversial. Hence, the reported incidence of IMN metastasis varies greatly.[4]

Adjuvant irradiation of the internal mammary lymph nodes (IMNI) represents the most important local therapy of this critical part of the lymphatic drainage system.[5,6] IMNI is recommended in case of macroscopic IMN metastases but is more commonly administered as part of "elective" regional nodal irradiation (RNI) when axillary lymph node metastases are present without clinically apparent IMN involvement. Previous studies have shown that including IMNI can improve overall and cancer-specific survival in these patients.[7,8]

Even though modern radiation therapy practices such as volumetric arc therapy and deep inspiration breath hold reduce the additional doses to the surrounding organs, IMNI is often associated with a higher radiation dose in organs at risk, such as the heart and the lung, due to its anatomic proximity.[9] This is critical as it is known that the probability of side effects such as major coronary events follows a linear dose-effect relationship.[10] Hence, routine inclusion of "elective IMNI" as a part of RNI remains controversial.[9,11] Neither the National Comprehensive Cancer Network nor the European Society for Medical Oncology guidelines define clear criteria for IMNI.[12,13] Instead, they recommend that "patient selection should consider risks versus benefits including long-term organ (cardiac and lung) toxicities, comorbidities of the patient, age, and life expectancy."[12,13]

However, estimating the benefit of IMNI is difficult. In the Danish Breast Cancer Cooperative Group trial, the effect of IMNI was more pronounced in patients at high risk of internal mammary node metastasis. In the recently published KROG 08-06 study, an overall survival benefit for elective IMNI was only shown for patients with medial and central tumors, a factor known to be associated with occurrence of IMN metastases.[7,8,14,15] Based on this, some guidelines recommend elective IMNI only for central and medial tumors.[16,17] Even though there is evidence for a higher risk of IMN involvement in medial or central tumors,[18,19] it should be noted that surgical studies have found positive IMN in up to 18% of patients with lateral tumors,[2] and lymphatic drainage to the IMN can be found in 29.5% of patients.[1] Among medial and central tumors, on the other hand, a large proportion of patients (48.0%-76.3%) show no drainage to the IMN.[1]

The individual lymphatic tumor drainage can be assessed using lymphoscintigraphy with direct tumor infiltration and a spatial resolution achieved with single-photon emission computed tomography (SPECT/CT).[20,21] Due to its demanding technical requirements, this procedure is often impractical for routine clinical implementation. As lymphatic pathways follow venous blood drainage, analyzing blood vessels in preoperative imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) could represent an alternative approach. Dynamic enhanced contrast MRI of the breast (DE-MRI) allows accurate diagnosis of the tumor and lymph nodes. Although DE-MRI is not routinely part of the primary diagnostics of patients with breast cancer, due to its higher sensitivity compared with mammography, it is widely used in screening of patients with *BRCA* mutation, young women, or other patients with high tissue density.[22] Moreover, in the case of suspect axillary lymph nodes, DE-MRI is often used to search for the presumed primary tumor of the breast.

Beyond its diagnostic value regarding the tumor and lymph nodes, DE-MRI brings additional information about the vascular environment. In the current study, we investigated the association between tumor contact with the internal mammary perforator vessels (IMPV) and the occurrence of ipsilateral and contralateral IMN metastases. We hypothesized that investigating the vascular environment could be superior for predicting gross IMN involvement compared with conventional risk factors such as tumor site.

Methods and Materials

Assessment and evaluation of all patient data were performed pseudonymized in our institution. The study was approved by the local ethics board (2023-118-S-NP).

Patient collective

For this retrospective study, we searched our institutional picture archiving and communication system (PACS) for patients with primary diagnosed breast cancer with pretreatment DE-MRI between 2011 and 2023, yielding inclusion of 527 patients. Among these, 58 (11.0%) had radiologically diagnosed gross ipsilateral IMN metastasis (iIMN+), 1 (0.2%) had bilateral IMN metastasis, and 229 (43.5%) had ipsilateral axillary (level I-IV) lymph node metastasis (AXN +) without IMN metastasis (IMN−). A total of 230 (43.6%) patients had no lymph node metastasis in the internal mammary region or the axilla (IMN−/AXN−). In addition, we included 9 patients with gross contralateral IMN metastases (cIMN+) diagnosed with DE-MRI and/or positron emission tomography/computed tomography (PET/CT) with no further distant metastases at time of staging. Patient characteristics are summarized in Table 1.

Table 1 Characteristics of patients with ipsilateral (iIMN+) or contralateral (cIMN+) internal mammary lymph node metastases compared with patients without internal mammary lymph node metastases (IMN−) with or without axillary lymph node metastases (AXN+/−)

Characteristic		IMN+				IMN−				Total	
		iIMN+ n = 59		cIMN+ n = 10		AXN+ n = 229		AXN− n = 230		N = 527	
		No.	%	No.	%	No.	%	No.	%	No.	%
Tumor location	Medial	13	22.0	1	10.0	23	10.0	34	14.8	70	13.3
	Central	14	23.7	2	20.0	59	25.8	63	27.4	138	26.2
	Lateral	17	28.8	2	20.0	100	43.7	96	41.7	215	40.8
	Multicentric	15	25.4	4	40.0	47	20.5	37	16.1	103	19.5
	Missing	-	-	1	10.0	-	-	-	-	1	0.2
Molecular subtype	HR+/HER2−	23	39.0	2	20.0	103	45.2	143	62.2	271	51.4
	HR+/HER2+	16	27.1	1	10.0	34	14.9	27	11.7	78	14.8
	HR−/HER2+	4	6.8	3	30.0	35	15.4	11	4.8	53	10.1
	TNBC	16	27.1	3	30.0	56	24.6	49	21.3	123	23.3
	Missing	-	-	1	10.0	1	0.4	-	-	2	0.4
Initial tumor size (T)	1	8	13.8	1	10.0	49	21.7	146	63.5	204	38.7
	2	31	53.4	-	-	116	51.3	78	33.9	225	42.7
	3	9	15.5	3	30.0	42	18.6	4	1.7	58	11.0
	4	10	17.2	3	30.0	19	8.4	2	0.9	33	6.3
	Missing	1	1.6	3	30.0	3	5.1	-	-	7	1.3
Differentiation (G)	1	3	3.5	-	-	8	3.6	36	15.7	47	9.1
	2	21	35.6	4	40.0	121	54.5	138	60.0	284	53.9
	3	35	59.3	5	50.0	93	41.9	52	22.6	184	34.9
	Missing	-	-	1	10.0	7	3.1	4	1.7	12	2.3
Affected breast	Left	32	54.2	8	80.0	134	58.8	105	54.3	279	52.9
	Right	25	42.4	2	20.0	91	39.7	125	45.7	242	45.9
	Both	2	3.4	-	-	4	1.7	-	-	6	1.1
Age (y)		Median (range)	48.3 (24.1-77.6)	Median (range)	58.9 (35.6-77.8)	Median (range)	49.6 (26.1-86.1)	Median (range)	48.6 (26.7-82.3)	Median (range)	48.3 (24.1-86.1)

Abbreviations: cIMN+ = involvement of contralateral internal mammary lymph nodes; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; iIMN+ = involvement of ipsilateral internal mammary lymph nodes; IMN−/AXN+ = involvement of axillary lymph nodes without positive internal mammary lymph nodes; IMN−/AXN− = absence of any lymphatic metastasis; TNBC = triple-negative breast cancer.

Evaluation of lymph nodes

The evaluation for the presence of gross internal mammary and/or axillary lymph node metastases was done by specialized breast cancer radiologists. For the assessment of internal mammary lymph node metastases, the size of the lymph node (with nodes larger than 5 mm raising suspicion), the shape, margins, number, presence of a fatty hilum, contrast enhancement, comparison with previous images, and, if available, diffusion information were considered.[4] Additionally, all clinical information and results from other examinations like ultrasound or PET/CT available at the time of the examination were included.

Assessment of primary tumor contact with ipsilateral IMPV

Using pretreatment DE-MRI scans with all available data including the maximum intensity projection (MIP), we explored the contact of the tumor with the ipsilateral IMPV (iIMPV) and classified the tumor vessel contact as follows (Fig. 1):

1. Major contact of the tumor with the iIMPV defined as either
   a. Contact of the tumor with multiple (≥5) IMPV side branches or

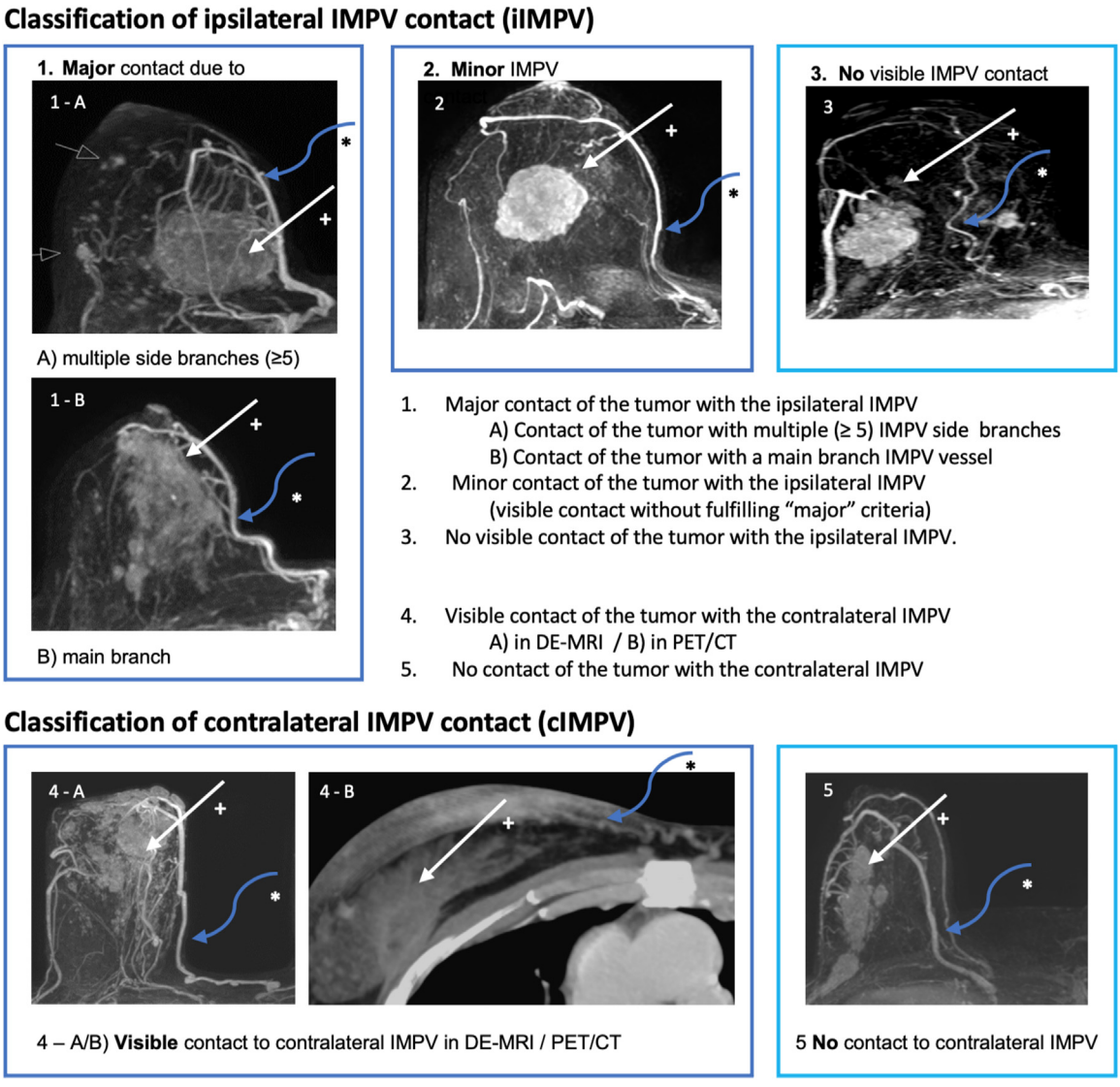


Fig. 1. Classification of tumor contact with ipsilateral IMPV: 1. (A) Major iIMPV contact due to multiple side branches, (B) major iIMPV contact due to main branch; 2. Minor iIMPV contact; 3. No visible iIMPV contact; 4. (A) Visible contact with cIMPV in DE-MRI, (B) visible contact with cIMPV on PET/CT; 5. No cIMPV contact. White straight arrows (+) label the breast cancer, blue curved arrows (*) label IMPV. *Abbreviations:* cIMPV = contralateral internal mammary perforator vessels; DE-MRI = dynamic contrast-enhanced magnetic resonance imaging; iIMPV = ipsilateral internal mammary perforator vessels; PET/CT = positron emission tomography/computed tomography.

b. Contact of the tumor with a main branch IMPV vessel
2. Minor contact of the tumor with the iIMPV, defined as visible contact without fulfilling "major" criteria
3. No visible contact of the tumor with the iIMPV

Unblinded assessment was carried out by a radiation oncologist (S.T.B.). In case of uncertainties, individual cases were discussed within the interdisciplinary team of radiologists and radiation oncologists.

Assessment of primary tumor contact with contralateral "crossing" IMPV

For all patients, we assesed the presence of "crossing" IMPV vessels from the contralateral side with contact to the tumor ("yes" or "no"; Fig. 1). Since DE-MRI was not available for all patients with contralateral IMN+, in 9 patients IMPV were analyzed in contrast-enhanced (PET-)CT images (Figs. 1).

Statistical analysis

The primary endpoint of this study was to investigate whether there is a statistically significant association of tumor contact with iIMPV and the occurrence of ipsilateral IMN metastases irrespective of tumor site. Further, we hypothesized that tumor contact with IMPV is a better predictor of gross IMN involvement compared with conventional risk factors such as grading, tumor size, tumor site, and molecular subtype. As a second endpoint, we aimed to investigate whether tumor contact with the contralateral IMPV is a risk factor for contralateral gross IMN metastases.

Data collection and statistical analysis were conducted using IBM SPSS Statistics version 26 and R version 4.2.3 (R Foundation for Statistical Computing). The differences between tumor-vessel contact of IMN+ (ipsilateral or contralateral) and IMN− (AXN+/−) patients were tested for statistical significance using the χ^2/Fisher exact tests and the McNemar-Bowker test depending on the structure of the data. Statistical significance was defined as $P < .05$.

Association of tumor contact with iIMPV with ipsilateral IMN+

In a first step, to compare the frequency of iIMPV contact, we performed a matched pair analysis of iIMN+ and iIMN − to account for different patient characteristics. Mandatory matching criteria were tumor location and molecular subtype. Initial tumor size and grade of differentiation were matched as best as possible. Patients who could not be matched within the mandatory criteria were excluded for this analysis (n = 2). The complete patient characteristics of the matched pair patient collective (n = 171) are summarized in Table 2.

In a second step, to compare the impact of different risk factors, we performed binary univariate and multivariate logistic regression including the following variables: tumor location (medial/central vs lateral), size (T1/T2 vs T3/T4), grade of differentiation (G1 vs G2/G3), hormone receptor status (HR negative vs HR positive), iIMPV contact (minor vs none), and iIMPV contact (major vs none). Discrimination was assessed using the area under the receiver operating characteristic curve (ROC).

Association of tumor contact with contralateral IMPV with contralateral IMN+

Due to the small number of cIMN+ patients, groups were compared without matching pairs. Furthermore, we performed binary univariate and multivariate logistic regression including all patients (N = 527) with contralateral (cIMN+), ipsilateral lymph node metastases (iIMN+ and iIMN−/AXN+) or without lymph node metastasis (IMN −/AXN−) and assessed the area under the ROC curve.

Results

Association of iIMPV contact with occurrence of IMN+

In the complete cohort, 100% of iIMN+ patients had an iIMPV contact; 94.9% (n = 56) of these were classified as major IMPV tumor contact. In iIMN−/AXN+ patients, on the other hand, major iIMPV contact was detected in only 29.3% (n = 67), and 30.6% (n = 70) had no iIMPV contact. In IMN−/AXN− patients, major IMPV contact was detected in 21.3% (n = 49) of patients whereas 41.7% (n = 96) of patients had no visible IMPV contact (Table 1). In the matched pair analysis, which compensated for different characteristics among iIMN− and iIMN+ patients (eg, tumor location, differentiation), the differences of tumor contact with iIMPV between iIMN+ and iIMN− (AXN +/AXN−) were highly significant ($P < .001$). Even when stratified by tumor location, the differences were still significant for all subgroups. The results for the matched pair analysis are delineated in Figure 2.

In univariate binary logistic regression, we found tumor location (medial/central vs lateral; odds ratio, 1.84; 95% CI, 1.03-3.41; $P = .04$) and tumor size (T3/4 vs T1/2; odds ratio, 2.84; 95% CI, 1.51-5.13; $P < .001$) to be significantly associated with gross IMN involvement. Due to the perfect prediction of the dependent variable by IMPV contact, multivariable regression analyses including IMPV contact were omitted. A multivariable regression analysis of the remaining variables (tumor size, grade of differentiation, or HR status) can be found in Table E1. In the ROC, iIMPV contact reached an area under the curve (AUC) of 0.85 (95% CI, 0.83-0.88), which was higher compared with a multivariate model including tumor location, grade of

Table 2 Patient characteristics for matched pair analysis: iIMN+ (left; n = 57), IMN−/AXN+ (central; n = 57), and IMN−/AXN− patients (right; n = 57) (total n = 171)

Characteristic		*iIMN+ (n = 57)*		*IMN−/AXN+ (n = 57)*		*IMN−/AXN− (n = 57)*	
		No.	%	No.	%	No.	%
Tumor location	Medial	11	19.3	11	19.3	11	19.3
	Central	14	24.6	14	24.6	14	24.6
	Lateral	16	28.1	16	28.1	16	28.1
	Multicentric	16	28.1	16	28.1	16	28.1
Molecular subtype	HR+/HER2−	24	42.1	24	42.1	24	42.1
	HR+/HER2+	14	24.6	14	24.6	14	24.6
	HR−/HER2+	4	7.0	4	7.0	4	7.0
	TNBC	15	26.3	15	26.3	15	26.3
Initial tumor size (T)	1	8	14.0	11	19.3	33	57.9
	2	31	54.4	29	50.9	20	35.1
	3	9	15.8	13	22.8	3	5.3
	4	9	15.8	3	7.0	1	1.7
Differentiation (G)	1	3	5.3	3	5.3	8	14.0
	2	21	36.8	29	50.9	34	59.7
	3	33	57.9	24	42.1	15	26.3
Affected breast	Left	32	56.1	33	57.9	25	43.9
	Right	23	40.4	24	42.1	32	56.1
	Both	2	3.5	-	-	-	-
Age (y)		Median (range)	48.3 (24.1-77.6)	Median (range)	46.2 (26.1-72.9)	Median (range)	48.8 (29.7-82.3)

Abbreviations: HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; iIMN+ = involvement of ipsilateral internal mammary lymph nodes; IMN−/AXN+ = involvement of axillary lymph nodes without positive internal mammary lymph nodes; IMN−/AXN− = absence of any lymphatic metastasis; TNBC = triple-negative breast cancer.

differentiation, molecular subtype, and tumor size (AUC, 0.65; 95% CI, 0.58-0.72) (Fig. 3a).

Contralateral IMN+ patients

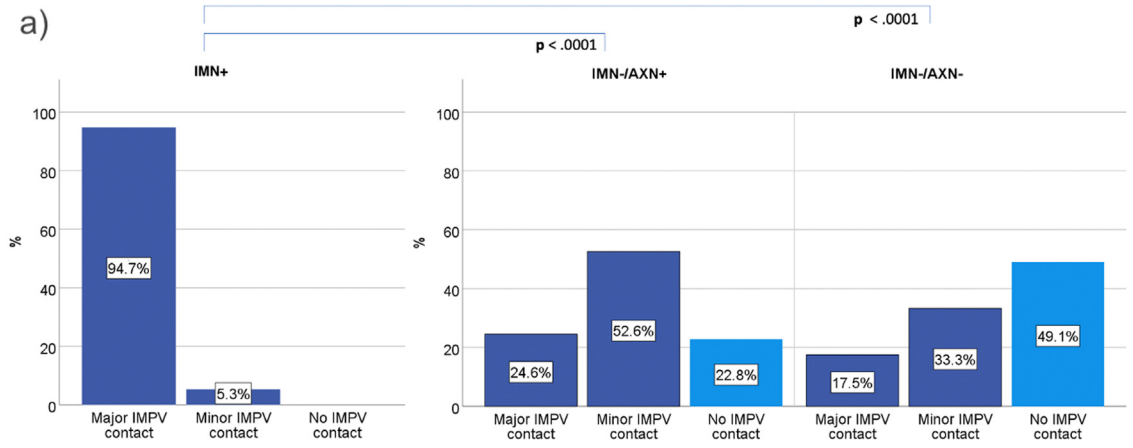
In all cases with contralateral IMN+ (100%), we detected tumor contact to crossing IMPVs from the contralateral side. In comparison, in patients without contralateral lymph node metastases, tumor contact with contralateral crossing IMPV was detected in only 53.4% (iIMN+), 26.2% (IMN−/AXN+), and 23.5% (IMN−/AXN−). The differences between these groups were also statistically significant ($P < .005$; Fig. 4). The AUC of contralateral IMPV contact alone for the prediction of cIMN+ was 0.92 (95% CI, 0.86-0.98; Fig. 3b).

Discussion

The present study has 2 key findings: First, our results show a highly significant association between ipsilateral gross IMN involvement and tumor contact with iIMPV in pretreatment DE-MRI of the breast. Interestingly, this effect was found to be irrespective of tumor location, indicating an independent and previously unexplored risk factor for iIMN+. In our study, major IMPV contact was superior in predicting iIMN+ compared with a multivariate model including conventional risk factors (tumor size, grade of differentiation, tumor location, and molecular subtype).

Second, the existence of visible crossing IMPV from the contralateral side to contact with the tumor appears to be a risk factor for contralateral gross IMN involvement. This finding reinforces the hypothesis that there is a relationship of lymphatic drainage with DE-MRI detected vascular pattern and further raises the question of whether the contralateral IMN region needs to be considered as part of the locoregional lymphatic drainage system in breast cancer.

Lymphatic vessels usually accompany larger blood vessels of the body. This also applies to the IMPV of the breast.[23,24] Therefore, it can be assumed that lymphatic drainage in patients with breast cancer can be predicted based on the vascular supply pattern of the breast. However, to our



b)

Ipsilateral IMPV contact		IMN+				IMN-/AXN+					IMN-/AXN-				
		Major IMPV contact	*Minor IMPV contact*	*No IMPV contact*	*total*	*Major IMPV contact*	*Minor IMPV contact*	*No IMPV contact*	*total*	*p*	*Major IMPV contact*	*Minor IMPV contact*	*No IMPV contact*	*total*	*p*
Location	**medial**	10	1	0	11	2	5	4	11	.0019	3	6	2	11	.001
	central	14	0	0	14	3	7	4	14	< .0001	7	5	2	14	< .0001
	lateral	14	2	0	16	2	10	4	16	< .0001	14	1	1	16	< .0001
	multicentric	16	0	0	16	7	8	1	16	.0008	4	7	5	16	< .0001
total		54	3	0	57	14	30	13	57	< .0001	28	19	10	57	< .0001

Fig. 2. Matched-pair analysis. (a) Contact of the tumor with ipsilateral IMPV in ipsilateral IMN+, IMN−/AXN+, or IMN −/AXN− patients. (b) Contact of the tumor with ipsilateral IMPV in IMN+, IMN−/AXN+, and IMN−/AXN− patients stratified by tumor location. *Abbreviations:* AXN+ = gross involvement of axillary lymph nodes; AXN− = negative axillary lymph nodes; IMN+ = gross involvement of internal mammary lymph nodes; IMN− = negative internal mammary lymph nodes; IMPV = internal mammary perforator vessels.

knowledge, there are no existing data on the correlation of lymph node metastases and vascular supply patterns in preoperative contrast-enhanced imaging in patients with breast cancer.

DE-MRI of the breast enables accurate illustration of individual anatomy of the breast with its blood vessels.[25] Furthermore, the use of DE-MRI is becoming increasingly common in pretreatment diagnostics, making it readily available for analysis. Our research findings indicate that gross IMN involvement can be predicted based on visualization of tumor vessels in pretreatment imaging. Interestingly, the analysis showed that tumor contact with the internal mammary lymphatic vessels alone was a superior predictor for gross IMN involvement compared with a multivariate model incorporating conventional risk factors. This raises the intriguing possibility that incorporating pretreatment MRI analysis could also improve the estimation of risk of microscopic involvement or undetected IMN metastases in clinically IMN− patients and help to select patients for IMNI. Nevertheless, it is crucial to emphasize that this hypothesis is speculative and lacks support from the current study, which only demonstrated a correlation between IMPV contact and gross IMN involvement. Therefore, further evaluation in prospective studies is warranted.

In addition, tumor contact with the contralateral IMPV that originates from the contralateral IMN was highly predictive of contralateral gross IMN involvement. Thus, it can be hypothesized that "crossing" IMPV is associated with atypical lymphatic drainage to the contralateral internal mammary region. Although lymphatic tumor spread to the contralateral axillary nodes is well described,[26] literature regarding contralateral IMN drainage and involvement is sparse. An anatomic study published 1932 found lymphatic connection between internal mammary chains in 9% to 17% of a healthy cohort, suggesting that contralateral IMN drainage is present in a relevant number of patients.[27] Accordingly, in their 2019 published study on CT-graphically determined incidence of IMN,[28] Singh et al detected bi-/contralateral IMN involvement in 9.1% of patients with locally advanced breast cancer. Furthermore, in a 1999

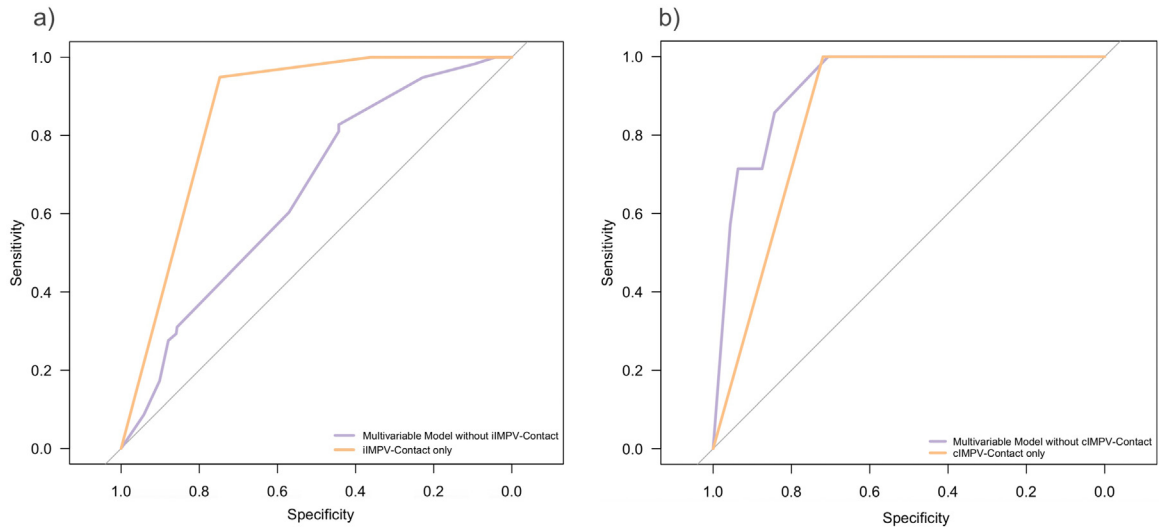


Fig. 3. ROC analysis for (a) predicting gross ipsilateral involvement of internal mammary lymph node metastasis with a multivariable model with conventional risk factors (without iIMPV contact) and iIMPV contact only and (b) predicting contralateral IMN+ with a multivariable model with conventional risk factors (excluding cIMPV contact) and cIMPV contact only. *Abbreviations:* cIMPV = contralateral internal mammary perforator vessels; IMPV = ipsilateral internal mammary perforator vessel; ROC = receiver operating characteristic.

lymphoscintigraphic investigation, Bourgeois et al detected invasion of contralateral IMN in 15.6% (n = 159) of 1025 patients with breast cancer.[29] In a 1988 radiologic study with a rather unfavorable patient collective, Scatarige et al found bilateral IMN involvement in 29% (n = 13) of patients with breast cancer with radiographically enlarged nodes (20.5%, n = 45 of 219).[30] Despite the existing evidence for regional lymphatic drainage to the contralateral IMN, this region has not been considered thus far during the adjuvant treatment of breast cancer. The fact that in our investigation all patients with contralateral IMN had crossing IMPV from the contralateral side supports the hypothesis that this vascular pattern may be an indicator for the risk of metastatic spread to the contralateral IMN. In our study, contact with the contralateral IMN was present in 33% to 54% of nodal positive patients. Further studies are needed to better understand the lymphatic drainage to the contralateral IMN in nodal positive patients and to investigate if treatment adjustment is required in case of high risk for contralateral drainage.

A potential limitation of the current study is that the diagnosis of IMN metastasis was based on MRI only (instead of histopathologic findings). It is known that relevant interobserver variability exists for the definition of IMN metastases on MRI as consensus definitions are lacking.[4] Also, the single center analyses and the rating of IMPV contact by a single observer are potential limitations.

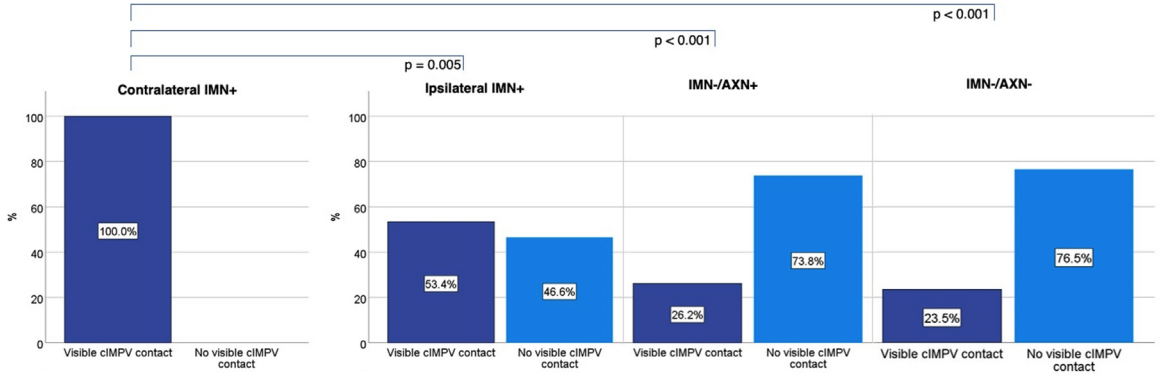


Fig. 4. Contact of the tumor with contralateral IMPV in patients with contralateral IMN+, ipsilateral IMN+, IMN−/AXN+, or IMN−/AXN−. *Abbreviations:* AXN+ = gross involvement of axillary lymph nodes; AXN− = negative axillary lymph nodes; cIMPV = contralateral internal mammary perforator vessels; IMN+ = gross involvement of internal mammary lymph nodes; IMN− = negative internal mammary lymph nodes.

Conclusion

We herein identified contact of the tumor with the iIMPV in pretreatment DE-MRI as an independent risk factor for gross IMN involvement in patients with locally advanced breast cancer irrespective of tumor location and other conventional risk factors. Furthermore, tumor contact with crossing IMPV appears to be a risk factor for contralateral IMN drainage. Prospective studies are warranted to assess whether tumor contact with IMPV correlates also with microscopic IMN involvement and whether this risk factor could aid selection of patients with breast cancer for IMNI.

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