MRI characterization of dissected sentinel lymph nodes of breast cancer patients at 7T

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Introduction: Breast cancer is the most common form of cancer in women worldwide. Axillary lymph node status is the most important factor determining prognosis. Assessment of nodal status requires surgical resection. First a sentinel lymph node biopsy (SLNB) is performed, which, if positive for metastasis, is followed by a complete axillary lymph node dissection. Both procedures are associated with morbidity and, in retrospect, are often performed unnecessarily. We have initiated a trial comparing non-invasive 3T MR imaging-based staging to surgical staging of axillary nodes. The performance of the in vivo performed MRI is controlled by 7T ex vivo MRI of all surgical specimens, which is followed by a node-to-node matching to pathology. This abstract describes the results of 7T MRI characterization of dissected sentinel lymph nodes of breast cancer patients, which have been correlated to pathology.

Material and Methods: We included 20 consecutive patients about to undergo a SLNB for the work-up of a histologically proven breast cancer with a diameter of at least 2cm, as determined on mammography and ultrasound. Following the SLNB, the nodes were conserved in formaldehyde, and stitched close together onto a plastic rack in order to maintain a consistent shape and achieve accurate shimming. During 7T MRI (Philips Health Care, Cleveland, USA), using a T/R head coil with a 16 channel receive coil (Nova Medical Systems), the nodes were submersed in fomblin to provide susceptibility matching. The scan protocol consisted of a 3D T1 weighted fat suppressed fast field echo (fsFFE) [TR/TE 158/5.59ms, flip angle 35º, FOV 23.6x110x110mm, resolution 0.18mm isotropic]; a T1-map, obtained with a 2D Look-Locker sequence [TR (between inversions) 4000ms, TE 3.72ms, flip angle 3º, FOV 5x110x110mm, in plane resolution 0.5mm, 100 samples with an increment of 40ms, initial TI 18ms]; a 3D T2-map, obtained from a multi-echo spin echo sequence [TR/first TE/ΔTE 13618/30/30ms, 8 echoes, FOV 24x110x110mm, resolution 0.5mm isotropic]; a 3D T2*-map, obtained from a multi-echo gradient echo sequence [TR/first TE/ΔTE 136/4.96/4.96ms, 10 echoes, flip angle 30º, FOV 24x110x110mm, resolution 0.35mm isotropic] and a 3D diffusion weighted image [TR/TE 4000/74.1ms, FOV 24x110x110mm, resolution 1.0mm isotropic, b-values 0, 750 and 1500s/mm^2]. The mean absolute T1, T2 and T2* relaxation times and the apparent diffusion coefficients (ADC) were determined for all nodes based on hand-drawn ROIs. Nodal dimensions were determined in 3 orthogonal planes. The presence of a fatty hilus was scored. Pathological processing and examination were performed by an experienced pathologist. To maintain an accurate correlation of MRI with pathology, the superior and one lateral side of each node were dyed black and blue respectively. The nodes were sliced in 4mm sections and numbered. They were paraffin embedded, cut into 3µm thick slices and stained with Haematoxylin & Eosin (H&E). Statistical analyses was performed by means of a logistic regression analyses according to the generalized estimating equations method.

Table 1.	Non-metastatic	Metastatic	Significance (P<0.05)
T1 Mean (±SD)	1454.5 (557.3)ms	1569.5 (661.0)ms	0.167
T2* Mean (±SD)	14.9 (1.8)ms	18.6 (4.8)ms	0.012
T2 Mean (±SD)	30.0 (2.9)ms	33.9 (8.1)ms	0.025
ADC Mean (±SD)	0.11·10^{-3} (0.1) mm^2/s	0.11 ·10^{-3} (0.1) mm^2/s	0.906
wxhxd Mean(±SD)	873.1 (1203.4)mm^3	1725.2 (1211.2)mm^3	0.229

Table 1. 7T relaxation times, ADC and "width x height x depth" (wxhxd) of all nodes.

Results: 83 nodes were excised and scanned. All MRI findings were correlated with the pathology results. 66 nodes were benign, 17 nodes contained metastases, of which 2 were micro metastases (<2mm). Table 1 shows the lymph node relaxation times, the ADC and the width x height x depth (wxhxd) for all nodes. 77% of the benign nodes and 64% of the malignant nodes had a fatty center. On the 3D-T1W-fsFFE scans lymph- and blood vessels were identified, as well as a metastasis inside a lymph vessel (figures 1-5). However the location of metastases inside the nodes could not be delineated morphologically.

Conclusion & Discussion: There was a significant difference in T2 and T2* relaxation times between metastatic and non-metastatic nodes. In addition, the very high resolution scans allowed for detection of a small in-transit metastasis inside a lymph vessel. There was no significant difference between the two groups in nodal dimensions, nor in T1 relaxation time or ADC. Furthermore both groups contained lymph nodes with fatty- and lymph nodes with non-fatty centers. Metastatic and non-metastatic nodes could not be discriminated from each other based on morphological criteria alone. For the 3T MRI *in vivo* part of this study all patients received i.v. injection of gadofosveset, a gadolinium-based contrast agent. It should be noted that although SLNB took place 4 days after the 3T MRI scan, we cannot completely exclude the possibility that the differences in transverse relaxation times at subsequent 7T are at least in part due to the presence of residual gadofosveset. This possibility is further explored, using the *in vivo* data, in a separate abstract.

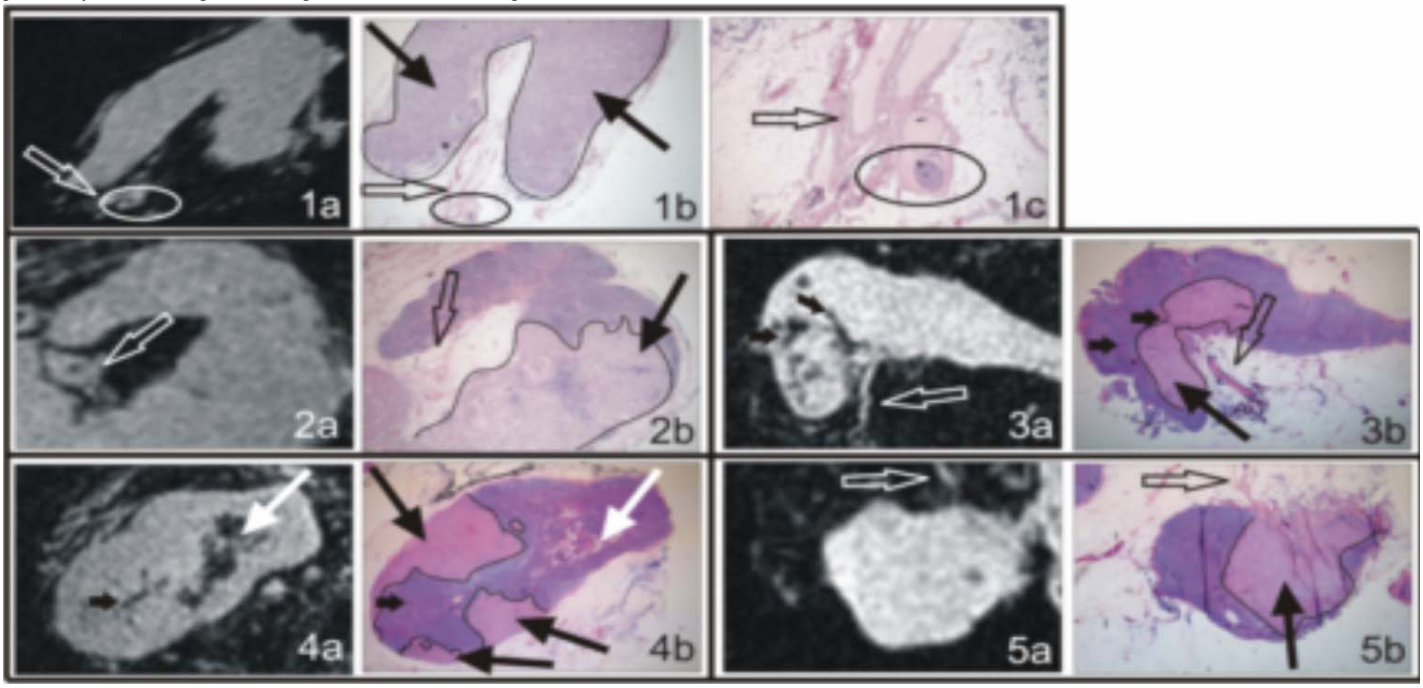

Fig 1-5; Correlation of 3D T1W-fsFFE images(180µm thick slices) to H&E stained histopathology images (1.5x magnification) **Fig. 1a.** A lymph node completely invaded with metastasis (black arrows). Efferent lymph vessels are depicted by the open arrow. Inside efferent lymph vessel is a small metastasis (circle). The lymph vessels have high signal intensity due to the fluid content. **Fig 1c** is a 5x magnification of the metastasis in the lymph vessel. **Fig. 2-5.** Four different lymph nodes which are all partially invaded by metastasis (large black arrows). On MRI there is no difference visible in signal intensity between the invaded and non-invaded part of the nodes. Efferent lymph vessels are shown by open arrows. In **figure 3 and 4** intranodal blood vessels are shown by small black arrows. Blood vessels have low signal intensity on MRI due to the iron content of the erythrocytes inside the vessels. In **fig.4** the white solid arrow depicts cortical fat.