HISTOLOGICAL DISTRIBUTION OF MAGNETIC NANOPARTICLES IN SENTINEL LYMPH NODES IN BREAST CANCER

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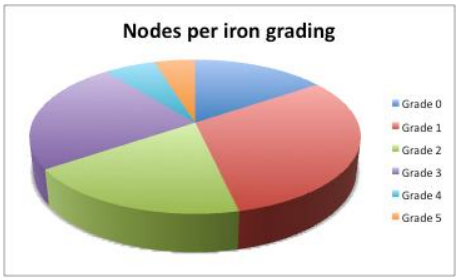
Background. There is growing interest in the use of magnetic resonance imaging (MRI) for pre-operative staging of the axilla in breast cancer. Evolving technology allows acquisition of high-resolution scan slices of 1mm thickness with the spatial resolution well within the range to detect micrometastases in lymph nodes. Administration and uptake of MRI contrast agents within the node itself may aid in the differentiation of abnormal from normal lymph nodes, which in the context of breast cancer, may significantly alter patients' surgical management.

Aim. To demonstrate the distribution of iron oxide nanoparticles histologically in metastasis-free and metastasis containing sentinel lymph nodes (SLN) following subcutaneous injection of superparamagnetic iron oxide nanoparticles (SPIO) in patients with breast cancer.

Method. Consecutive patients with breast cancer undergoing SLN biopsy were invited to consent to injection of 2mL of Endorem (Guerbet, Paris) at the circumareolar margin of the upper outer quadrant of the affected breast pre-operatively. The SLN was identified intra-operatively using the combined technique of radioisotope (Technetium^{99m}) and blue dye (Guerbet, Paris). Each SLN was examined *ex-vivo* by a consultant histopathologist for the presence of iron and the distribution of iron particles within the node. Presence of iron was graded from 0 to 5 (0 - no iron seen, 5 - extensive iron distribution throughout). The distribution of iron whether trapped within the macrophages or free within the node was noted as was the anatomical position where the iron had deposited. Select nodes underwent further PERL staining specifically to detect the presence of iron for comparison with the appearance of the nodes after H&E staining only as per routine histopathological practice.



Results. A total of 85 SLNs from 35 patients (and an additional node as a control) were examined for the presence of iron. The pie chart demonstrates the proportion of iron staining identified in each node using our grading system. Iron distribution was predominantly within the sinuses (72/85) with fewer nodes containing iron in the subcapsular space (9/85). In 12/85 nodes where iron was seen within the parenchyma, iron was also clearly seen within the sinus.

Of 13 involved SLNs, 9 contained a macrometastasis and one contained a micrometastasis. Nodes containing metastases had variable quantities of iron within them (grade 0 = 5 nodes, grade 1 = 8 nodes, grade 2 = 2 nodes, grade 3 = 1 node (micrometastasis)). The iron was not present in the area of the node containing the metastasis with the exception of one node where the entire node was replaced with metastatic tumour. This node had small amounts (grade 1) of iron throughout.

In 45/85 nodes (53%), iron was only seen within macrophages and 25/85 (29%) nodes contained iron both within macrophages and free. Iron was not seen in 14/82 nodes. The control node was graded 1, and contained iron within the macrophages in the sinuses of the node.

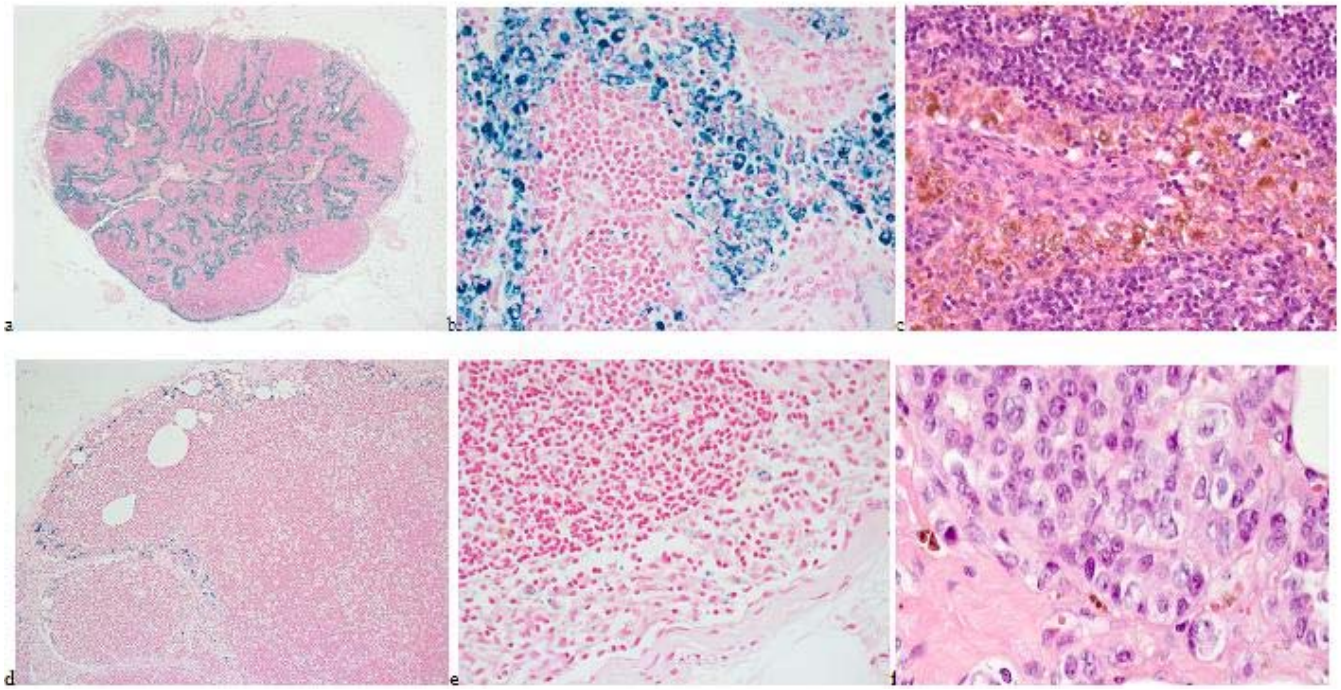


Image (a) Normal SLN with iron deposition in the sinuses seen with PERL staining (grade 5). (b) Magnification demonstrating extensive iron in macrophages and nodes in the sinus of a normal SLN with PERL staining. (c) As in b without PERL staining. (d) Normal SLN with grade 3 iron deposition within the sinus and the subcapsular space. PERL stained. (e) Normal SLN with grade 1 deposition of iron within the sub-capsular space. (f) Small amount of iron (grade 1) present within normal area of SLN. Metastasis containing area – upper half – remains iron free

Discussion

SPIO uptake in the SLNs anatomically following subcutaneous injection in the breast is variable. In SLNs with metastases, iron is not seen within the metastatic focus. With the increasing use of MRI for the assessment of the axilla following contrast administration, non-homogenous enhancing of the SLN may indicate a metastatic focus. With complete nodal destruction by metastasis there remains a small amount of uniform iron distribution throughout the node, however in this instance altered morphology, for example with loss of hilar fat, should be identified on MRI irrespective of iron distribution.