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Iron-oxide-enhanced MR lymphography: just a new toy or a breakthrough?

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Despite its proverbially high soft tissue contrast, unenhanced MR imaging is not capable of making the important distinction between normal or inflammatory lymph nodes, on the one hand, and lymph node metastases, on the other. This is so because there is wide overlapping of the T1 and T2 relaxivities of these tissues; nor does the use of unspecific contrast media improve MR imaging of lymph nodes.

Initial experimental results of MR lymphography following intravenous injection of ultrasmall superparamagnetic iron oxide particles were published by Weissleder and co-workers in 1990 [1]. What made these results spectacular at that time was the fact that an accumulation of contrast material in lymph nodes had not been observed before. Up to then, only direct injection of markers into the lymph nodes or into the interstitial space had been performed for radiographic and nuclear medi-

cine procedures as well as for experimental CT and MR imaging techniques.

Intravenous MR lymphography using ultrasmall superparamagnetic iron oxide particles is based on the physiological effect of particle extravasation in the peripheral vascular bed and their passage into the interstitial space, which occurs as a result of their small size. Transport of the particles from the interstitium into the lymph nodes is effected by mechanisms known from interstitial lymphography. A smaller part of the particles reaches the lymph nodes directly through the blood. The spectacular conclusion suggested by these observations was the potential of iron oxide particles to achieve opacification of all lymph nodes of an organism through a single systemic intravenous injection of contrast medium. The mechanism through which metastases are identified within lymph nodes is the same as that already known from the administration of iron oxide particles in liver imaging: The contrast medium is taken up by intact lymph nodes and produces a signal loss, whereas the signal of metastatic tissue remains unchanged; however, many problems have to be overcome before this simple, experimentally confirmed principle can be used in routine clinical imaging. This is also reflected in the article by Sigal et al. in this issue of “European Radiology”

[2] reporting the results of an extensive analysis of a multicenter study on the role of MR lymphography using ultrasmall iron oxide particles in the diagnostic assessment of lymph node metastases from squamous cell carcinomas of the head and neck area. Based on the above-described mechanisms of action, an impartial judge would expect the administration of iron oxide particles to improve the sensitivity of MR imaging in detecting lymph node metastases. But this was not the case in the study by Sigal et al. [2]. Sensitivity was already high in the precontrast examinations and could not be improved further by contrast medium administration; however, they found a marked improvement in specificity. This study as well as previous publications on iron-oxide-enhanced intravenous MR lymphography suggest that the contrast medium under investigation is ahead of its time. Besides the task of discriminating normal lymph node tissue from tumor tissue, diagnostic lymph node assessment is confronted with the problem of visualizing extremely small structures, which requires a very high spatial resolution of MR imaging. The most advanced MR imaging technology, such as phased-array coil systems, improves the potential for identifying small structures. Furthermore, a high resolution must be achieved in combination with an optimal susceptibility to effects of the

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contrast medium without inducing susceptibility artifacts. This requires additional fine adjustment of the sequences and parameters used. Furthermore, it is theoretically conceivable that the diagnostic accuracy of MR lymphography can be further improved by using higher field strengths. Increasingly more whole-body MR imaging units are being in-

stalled that operate at field strengths of 3 T or above. Although, at first glance, the results of the study under discussion are not positive throughout, they at least show that the principle of MR lymphography works. The pace at which MR imaging technology is developing at present makes it likely that the problems discussed by Sigal et al. [2], among

them the detection of very small metastases in small lymph nodes, local overdose artifacts, and motion artifacts, can be overcome in the future, and that intravenous MR lymphography using ultrasmall iron oxide particles will develop into a routine diagnostic procedure with a role in therapeutic decision making.

References

1. Weissleder R et al. (1990) Radiology 175:494
2. Sigal R, Vogl T, Casselmann J et al. (2002) Lymph node metastases from head and neck squamous cell carcinoma: MR imaging with ultrasmall superparamagnetic iron oxide particles (Sinerem MR) — results of a phase-III multicenter clinical trial. Eur Radiol 12:1104–1113