

USPIO enhanced diffusion MRI increases the diagnostic confidence for detection of pelvic lymph node metastases in patients with bladder or prostate cancer

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Introduction: The correct primary staging of bladder and prostate cancer using USPIO enhanced MRI for the assessment of lymph node metastases is not only limited due to the restricted size of the target but also undergoes a learning curve, is hampered due to various types of artifacts and is rather time-consuming [1-3]. Further on, micrometastases are present in 25% of patients with normal sized lymph nodes. Diffusion-weighted MRI (DW-MRI) after administration of USPIO seems to be promising as it allows combining functional and susceptibility effects to overcome some of the above mentioned drawbacks of lymph node assessment. In fact, malignant lymph nodes contrary to benign ones may be distinguished due to their remaining high signal intensity on DW-MRI, while the benign ones lose their signal following USPIO uptake. Potentially, the T2* sensitive DW-sequences therefore provide diffusion related cellular information [4] combined with USPIO uptake and distribution data in one single examination. Therefore in a preliminary prospective study the hypothesis that DW-MRI after administration of USPIO helps to increase the diagnostic confidence of normal sized lymph node staging in patients with bladder or prostate cancer was studied.

Materials and Methods: Twenty one patients (4 w, 17 m, median age: 63 years, range: 50-74) with bladder cancer (n=11), prostate cancer (n=8) or both (n=2) planned for surgical lymphadenectomy and giving informed consent were examined twice on a 3T MR unit (Trio, Siemens Medical, Erlangen, Germany) provided with body phased-array coils. For morphological evaluation a 3D T1-w and T2w- SPACE sequence (isotropic voxel size 0.75 mm³ and 1.0 mm³ respectively) were performed. Twenty four to thirty six hours after intravenous drip infusion of USPIO (Ferumoxtran, 2.6mg Fe/kg Sinerem, Guerbet, France) the MRI was repeated. In addition to the morphological pre-USPIO sequences a 3D T1-w VIBE in the coronal plane (TR 6ms, TE 2,41ms, isotropic voxel size 1.0 mm³, TA 2:51 min) and an axial DW-MRI sequence were performed (TR 4700ms; TE 59ms; 3 b-factors 0,500,1000s/mm²; matrix 128x128, FOV 330x330mm², slice thickness 4mm; TA 4:23 min). Image analysis was performed in consensus by 2-3 readers. First the morphological sequences were analysed. The main criterium for metastasis was an SNR-decrease on the T2-w sequences of less than 20% when comparing pre- and post USPIO images. A stronger SNR decrease reflects uptake of USPIO, but in certain cases might be locally limited when the lymph node is partially invaded by metastasis. The exact localisation of the suspected lymph nodes was marked on the VIBE sequences, allowing a better allocation to the pelvic vessels on demand of the surgeons. DW-MRI after USPIO was evaluated qualitatively. Focal zones of high signal intensity on the DW-MR images at a b-value of 1000s/mm² (b 1000 images) corresponding to lymph nodes on the morphological sequences (3D T1- or T2-w SPACE, 3D T1-w VIBE) were considered as malignant.

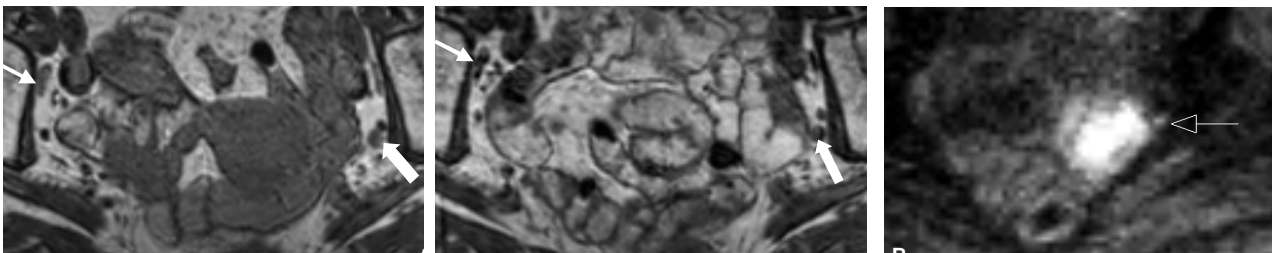


Fig: 79 y old patient with a bladder carcinoma: A: Axial reconstruction of a 3D T2-w SPACE sequence pre USPIO B: Identical axial plane acquired 24 hours after iv administration of USPIO C: Axial DW-MRI (b 1000) post USPIO. No significant SNR decrease (<20%) after USPIO in an obturator interne lymph node on the left side (large arrow on A and B) indicative for metastasis. Fig 1C shows the corresponding high intensity in DW-MRI after USPIO confirming metastasis. On the right side (smaller arrow on A and B) a normal lymph node with a significant SNR decrease after USPIO (A vs. B) is visible. This normal lymph node is not detectable on the DW-MRI due to susceptibility effects following USPIO uptake. Only malignant lymph nodes remain hyperintense on the DW-MRI sequences facilitating the reading.

Results: Twenty of 21 included patients underwent surgery with template lymphadenectomy of the entire pelvic region. One patient had to be excluded from surgery due to bone metastases, primarily detected on DW-MRI. According to histopathology as gold standard lymph node metastases were found in 5 of 20 patients. Fifteen were negative on histology (Tab). USPIO enhanced imaging alone correctly detected 4/5 patients as positive. In the remaining patient a micrometastasis of 0.4mm x 0.7mm in a lymph node of 3.5mm x 4mm size was missed (i.e. one false negative). USPIO imaging classified 4 patients as false positive. Finally, 11/15 negative patients, according to histopathology, were correctly detected as negative.

DW-MRI with 4/5 correct positive and one false negative patient yielded similar sensitivity results compared to USPIO. However, DW-MRI improved specificity by detecting 13/15 patients as correctly negative and only two as false positive.

Further on, clinical applicability of a method requires besides fast scan times also the possibility for fast processing: To evaluate the USPIO enhanced morphological sequences 1h 40min (range: 45-180 min) were required, while the analysis of the DW-MRI after USPIO lasted only approximately 10 min (range: 3-45min).

		Histopathology				Histopathology	
		positive	negative			positive	negative
USPIO MRI	positive	4	4	DW-MRI post USPIO	positive	4	2
	negative	1	11		negative	1	13

Tab: Diagnostic accuracy of USPIO enhanced morphological T2-w MRI (left) and DW-MRI post USPIO (right side) versus histopathology.

Conclusion: This preliminary clinical study indicates that DW-MRI together with USPIO helps to speed-up and facilitates the reading. It also improves the diagnostic confidence to detect lymph node metastases in normal sized nodes. However, DW-MRI needs always to be confirmed by the morphological imaging. DW-MRI enhanced USPIO is a promising technique to improve the lymph node staging of prostate or bladder cancers.

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References:

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