

Diagnostic Accuracy of Diffusion-weighted MRI in comparison to Histopathology for Detection of Lymph Node Metastases in Normal Sized Pelvic Lymph-nodes in Patients with Bladder or Prostate Cancer

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Introduction: Correct primary staging of bladder and prostate cancer including the assessment of lymph node metastases has a great impact on treatment and prognosis influencing even the long-term outcome of patients [1]. Conventional cross-sectional imaging (CT, MRI) based on morphology and size criteria have limited ability to predict such lymph node metastases. According to RECIST 1.1 criteria, threshold size for positive lymph node metastasis is defined as 10mm in case of bladder and 8mm for prostate cancer in the short-axis. It has been reported that the presence of metastases in occult lymph nodes in patients with bladder or prostate cancer and preoperative negative staging according to the above mentioned threshold criteria reaches a rate of 25% [2]. That means that pelvic lymph node dissection (PLND) still remains the gold standard for the detection of lymph node metastases in patients with urogenital cancers [3]. Trying to find new, more accurate, noninvasive methods for the detection of lymph node metastases especially in patients with normal sized lymph nodes would not only allow improving the preoperative staging of urogenital cancers but also promise improved surgical treatment. Therefore, the aim of the present study was to assess the diagnostic accuracy of Diffusion-weighted MRI (DW-MRI) for the detection of metastases in normal sized lymph nodes in patients with bladder or prostate cancer and negative staging according to the conventional CT/MRI and bone scintigraphy. The results were correlated to histopathology after meticulous template lymph node dissection.

Materials and Methods: Data reported here are parts of a larger prospective clinical trial aiming to include in total 120 evaluable patients. A total of 87 patients (7 w, 80 m, median age: 63 years, range: 43-82) with bladder cancer (n=23), prostate cancer (n=47) or both (n=4) planned for surgical lymphadenectomy and giving informed consent were examined on a 3T MR unit (Trio, Siemens Medical, Erlangen, Germany) provided with body phased-array coils. For morphological evaluation a 3D T1-w SPACE (TR 700ms, TE 16ms, isotropic voxel size 0.75 mm³, TA 7:06 min) and a 3D T2-w SPACE (TR 640ms, TE 47ms, isotropic voxel size 1.0 mm³, TA 8:27 min) were performed. Axial EPI DW-MRI sequences with 3b-factors (0, 500, 1000sec/mm²) and the following parameters (TR 4700ms, TE 59ms, matrix 128x128, FOV 330, slice thickness 4mm, 6 acquisitions, TA 4:23 min) were acquired.

Image analysis was performed twice, first prospectively in consensus by 2-3 readers before surgery and then several months later in a longer reading session independently by three other readers. For the second reading readers were blinded to all clinical data, any previous imaging study or histopathological results. The main criterium for metastasis was a hyperintensive, non-continuous structure on the high b-value images corresponding to a lymph node and with a low ADC value beyond 100x10⁻⁵ mm²/sec. Template lymphadenectomy was performed in all patients with separate sampling of all suspicious lymph nodes from the prospective reading. Histopathological correlation was performed on a per patient basis.



Fig: 74 year old female patient with a bladder carcinoma: A (left): Axial DW-MRI (b 1000) image with a hyperintensive structure close to the bladder (white arrow). B (middle): Identical axial plane representing the ADC map. The mean ADC of the lymph node (black arrow) was measured with 78×10^{-5} mm²/sec. C (right): Axial 3D T1-w SPACE reconstruction allowing to match the hyperintensive structure with a suspicious lymph node, which was correctly classified as positive from all readers. Size of the metastasis: 2mm x 2mm.

Results: 87 included patients accomplished the MRIs successfully and underwent surgery with template lymphadenectomy of the entire pelvic region. A total number of 3533 lymph nodes were resected and screened for metastases (41/patient). According to the reference standard lymph node metastases were found in 25 of 87 patients. Prospective DW-MRI enhanced imaging alone correctly detected 14/25 patients as positive. In the remaining 11 patients mostly micrometastasis in single lymph nodes with a size underneath 3mm were missed. DW-MRI classified 22 patients as false positive often due to overstaging of smaller hyperintensive structures. Finally, 40/62 negative patients, according to histopathology, were correctly detected as negative. The three independent readers achieved higher diagnostic accuracies with 75.9%, 88.5% and 88.5%, respectively. Their negative predictive values were excellent with 84.7%, 91.9% and 93.3%. Fleiss's kappa interrater agreement for the four ratings yielded a 77.8% overall agreement and a Randolph's free-marginal multirater kappa value of 0.55 corresponding to a moderate interrater agreement. This higher diagnostic accuracy in the second reading might be related to a learning curve of the readers.

Prospective reading	Histopathology		Independent Reading	First Reader	Second Reader	Third Reader		
	positive	negative					positive	negative
DW-MRI	positive	14	22	positive	16	9	20	5
	negative	11	40	negative	12	50	5	57

Tab: Diagnostic accuracy of the prospective DW-MRI reading (left) and the follow-up reading performed by three independent readers (right) in comparison to histopathology..

Conclusion: These preliminary results indicate that DW-MRI helps to improve the diagnostic confidence to detect lymph node metastases in normal sized nodes. However, it often remains difficult in case of small lymph node metastases which are missed due to poor spatial resolution or in case of unspecific impeded diffusion yielding a high number of false positive cases.

Acknowledgment: The work was supported by SNF 320000-113512

References:

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