Does quantification of T2 SNR decrease after USPIO administration allow differentiation between benign and malignant normal sized pelvic lymph nodes?

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Introduction:
Correct staging of prostate and bladder cancer is an important prerequisite for surgery and further treatment of the patient. Up to date the diagnosis of pelvic lymph node metastases is limited to size criteria only (by CT or MRI), however it has been shown that lymphotropic USPIO may improve the detection and differentiation of metastases nodes in patients with prostate or bladder cancer (1,2). Methodologically the large majority of previously published clinical studies are based on the qualitative analysis of signal decrease in lymph nodes occurring on T2/T2* weighted sequences after USPIO administration. Therefore, the aim of our study was to quantify lymph node signal intensity decrease (SI, SNR and CNR) and to assess whether a potential cut-off value might be defined to differentiate benign from malignant normal sized pelvic lymph nodes.

Methods:
Fifty-two patients (52 patients, 8 females, 44 males, mean age 62yrs; range 34-74yrs) with histological proven bladder (n = 18) and/or prostate cancer (n = 30; n = 4 with both) were examined on a 3T MR unit (Trio, Siemens Medical, Erlangen, Germany; with body phased array coils) before and 24-36 hours after USPIO. Lymph node signal intensity quantification was performed on a 3D T2w TSE SPACE sequence (isotropic voxels=1mm³; TR=640ms, TE=47ms, bandwidth 465Hz/pixel, time of acquisition: 8:27min) on pre- and post-contrast images. Signal-intensities (SI) were measured drawing freehand ROIs three times per lymph node in the axial orientation selecting the largest diameter. To determine signal-to-noise ratios (SNR) the following equation was employed: SNR = SI / STD-Noise. Extended template lymphadenectomy was performed in all patients allowing histopathological correlation.

Results:
In 52 patients a total of 2060 lymph nodes were resected. 320 of these nodes (57 inguinal; 263 iliacal) underwent MRI-post-processing by the above mentioned method. Fifty positive lymph node metastases were detected in 15 patients on histology. 20 of the larger lymph nodes (> 3mm; all iliacal) could be correlated with single lymph nodes on the T2-w 3D SPACE sequence. In proven malignant lymph nodes both mean signal intensities (with 1.03 % ± 14.5 %; range: +26% / -27.1%) and SNR (with 2.5 % ± 21%; range: +67/-27.1%) remained unchanged after the administration of USPIO. To the contrary, benign lymph nodes presented a mean SI decrease of 20%± 23.8% (inguinal) and of 24.4% ± 31.3% (iliacal)(range: -78.4/+274.8%). SNR decrease differed significantly (p=0.038) for inguinal (3.4% ± 55.4%) and iliacal lymph nodes (24.8% ± 54.6%; range: -92.9/+315%). Overlap of SNR changes were attributed to lipomatosis, partial voluming, histiocytosis and focal hyperplasia within lymph nodes.

Discussion and conclusions:
Our study results confirm as expected that both SI and SNR changes comparing benign and malignant normal sized pelvic lymph nodes yield significant differences (p=0.001; p=0.05). Malignant lymph nodes overall have little USPIO uptake which is also reflected in their almost absent SI or SNR decrease, respectively. Nevertheless definition of a cut-off value defining malignancy on a percentile level seems problematic due to high heterogeneity of data and substantial overlap of single results. Moreover, limitations such as the low number of exclusive intra-lymphatic voxels (related to the restricted size of the lymph nodes in question despite a rather high spatial resolution), overlay of fatty hilus without USPIO uptake and irregular morphology of the single nodes with elongated forms must be considered. Furthermore, inguinal lymph nodes compared to iliacal lymph nodes present a rather limited if not absent USPIO uptake. Therefore, it must be emphasized that staging of normal sized lymph nodes must include besides qualifying uptake of lymphotropic USPIO across the entire cross-section, various additional criteria such as morphology, fatty content or localisation of lymph nodes. Therefore SNR decrease quantification alone is not sufficient.

References:

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Fig 1, 2: Signal intensities pre- and 24-36 hours post USPIO administration within two lymph nodes (1,2): benign lymph node on the left with SI decrease from 86 to 13, while the malignant lymph node on the right presents a much reduced relative SI decrease from 189 to 126.

Fig 3, 4: Partially malignant lymph node pre- and post USPIO with limited signal decrease (285/253)