Lymph Node Imaging in Prostate Cancer

J.O. Barentsz,

This course will show the value of existing (MR) techniques in the detection of lymph node (LN) metastases in prostate cancer. Limitations of current diagnostic procedures will be highlighted, and potential new developments will be discussed.

The prognosis of patients with prostate cancer (PC) is poorer if LN metastases are present. The risk of LN metastases is currently determined (albeit inaccurately) using nomograms [1, 2]. Thus in patients with an elevated risk for metastasis, additional examinations are required. Today, the most commonly used imaging techniques for detecting LN metastases are multi-detector CT scan (MDCT) and conventional MRI, with image interpretation essentially based on LN size and shape criteria. Although the criteria vary slightly [3], LN with a short-axis diameter >8 mm for round LN and >10 mm for oval LN are generally considered to be malignant [4, 5]. Both MDCT [6] and MRI [7] have a low sensitivity (36 and 39%, respectively) for diagnosing prostate cancer LN metastases using these size and shape criteria. In studies that have employed thresholds as small as 6 mm [8], the specificity was very high (95-100%) but the sensitivity was too low (0-25%) to be useful in regular clinical practice for the evaluation of metastatic LN disease [9]. Some authors advocate restricting the application of these techniques to high-risk patients (e.g., with PSA levels >15 ng/ml, or Gleason >7, or stage T3) in order for them to be cost-effective [10, 11]. Thus, supplementary, invasive diagnostic examinations in the form of surgical pelvic lymph node dissection (PLND) are still commonly performed.

Magnetic resonance lymphography (MRL) using a lymph-node-specific contrast agent (Combidex/Sinerem) [12, 13] is an experimental technique that, compared to PLND, has a high negative predictive value (>96%) for the detection of lymph node metastasis in extended areas. Importantly, its use can render PLND unnecessary in negative cases [14]. Unfortunately due to regulatory issues the development of this contrast agent is continued. Nonetheless, the lessons we learned using this contrast agent are very interesting. First, routine PLND misses in 41% of patients their positive LN’s. Second, 50-60% of the patients had at least one MRL-positive lymph node outside the RTOG-CTV. To reduce geographical miss while minimizing toxicity, image guided definition of an individual target volume seems to be necessary [15, 16]. Third the Nodal Roach Formula (NRF) nomogram has a PPV of only 20% [17]. Fourth Seventy-nine percent of the PSA-recurrent patients had at least one aberrant positive LN outside the RTOG-CTV. Application of the standard RTOG-CTV for pelvic irradiation in the salvage setting therefore seems to be inappropriate. [18]. Fifth, MRL can be used to select patients with limited lymph node involvement for pelvic radiotherapy. MRL-guided delineation of a boost volume and an elective pelvic target volume for selective high-dose LN irradiation with IMRT is feasible. Whether this approach will result in improved outcome for these patients needs to be investigated in further clinical studies [19]. Sixth, MRL detected positive lymph nodes in 72% of candidates for salvage radiotherapy, and in 62% of candidates for early salvage radiotherapy. The Stephenson nomogram showed a good correlation with the MRL result and may thus be useful for identifying patients at risk for lymph node involvement [20]. Thus the extent of LN metastases in prostate cancer in greatly underestimated, thus improved imaging is needed.

Alternatives to Combidex/Sinerem MRI are ferumoxytol MRI, 11C PET-CT, and DWI. Comparison of Combidex/Sinerem with ferumoxytol MRI shows that ferumoxytol MRL has a significantly lower diagnostic accuracy, which potentially can result in an unacceptable number of false negatives.

11C-Choline PET-CT has shown to detect LN metastases with a mean size of 8 mm versus 5 mm in Sinerem/Combidex. Also, in significantly less patients LN metastases were detected: 23/29 patients versus 13/29 to Sinerem/Combidex and 11C-Choline PET-CT respectively
Finally, DWI has shown potential in the detection of LN metastases [21]. Based on a cut-off value of 1000 mm²/sec normal size metastatic LN could be differentiated from non-metastatic LN, based on its lower ADC-value. However, below the threshold of 5 mm this technique is still not reliable. Unfortunately the majority of positive LN are having a size < 5 mm. Thus further attempts to improve LN detection using specific molecular (MR) techniques are absolutely needed.

References


