

The enigma of lymph node staging in breast cancer

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Valorisation

Valorisation

Breast cancer is the most common type of invasive cancer among women worldwide, with an estimated 1.7 million cases and 521,900 deaths in 2012. In the Netherlands, the annual incidence is more than 14,000 patients. Nowadays, standard treatment consists of surgery of the breast and axilla, complemented with radiation and/or systemic therapy. This extensive treatment has led to a mean five year overall survival of 90%. Regarding the health care costs, breast cancer treatment represents approximately 15% of all health care costs in the Netherlands.

The excellent survival caused an attention shift from survival to the presence of morbidity and quality of life after treatment. Better patient selection for specific therapies and use of less invasive techniques, in order to avoid overtreatment on an individual level, aim to further minimize morbidity and complications of therapy and consequently reduce nationwide health care costs.

The aim of this thesis was to investigate the enigma of lymph node staging in breast cancer patients, by improving diagnostic accuracy of nodal staging in order to achieve a more patient-tailored treatment with minimal invasive therapy and reduced morbidity.

Relevance of scientific results in this thesis

Currently, axillary surgery is performed in every patient to investigate the axillary lymph node status. In clinically node negative patients sentinel lymph node biopsy (SLNB) is performed, whereas axillary lymph node dissection (ALND) is performed in clinically node positive patients. These procedures can cause complications, such as lymphedema, numbness and pain. In addition, patients without axillary lymph node metastases do not benefit from the axillary surgery, since they do not have any prognostic benefit from the procedure. Approximately 80% of clinically node negative patients and 40% of clinically node positive patients treated with neoadjuvant systemic therapy only have benign axillary lymph nodes. Yet, these patients are still exposed to axillary surgery with its concomitant complications.

This thesis explored further techniques to improve lymph node staging in breast cancer. We showed that patients with negative axillary findings on T2 weighted breast MRI, with a complete field of view of the axillary region, do not require any further diagnostic imaging. When compared to axillary ultrasound, T2

weighted breast MRI even improved differentiation between limited and advanced axillary nodal disease.

In clinically node positive patients treated with neoadjuvant systemic therapy, RISAS-procedure might become the new standard procedure to accurately identify axillary pCR. Previous studies already demonstrated less complications after SLNB as opposed to ALND. Consequently, ALND can be safely omitted in patients with axillary pCR according to RISAS, indicating these patients will experience less often any of the aforementioned surgical complications. Yet, final results of this Dutch prospective multicenter trials must confirm the validity of this technique first.

Finally, this thesis demonstrated that dedicated axillary ^{18}F -FDG hybrid PET/MRI is feasible in clinically node positive breast cancer patients to differentiate between limited and advanced axillary nodal disease. However, results of this technique should be further explored in research setting, before implementation into daily clinical practice is justified.

Target population

This thesis contributes to newly diagnosed breast cancer patients, by improving the diagnostic accuracy of axillary lymph node staging. In addition, results of this thesis are relevant for all physicians involved in treatment trajectories of breast cancer patients. Finally, dedicated axillary hybrid PET/MRI might encourage other researchers in the field of oncologic imaging in which lymph node staging is an important prognostic factor, such as melanoma, esophageal, ovarian, prostate and rectal cancer.

Innovation and future

Future studies should explore whether increasingly advanced imaging tools, like dedicated axillary hybrid PET/MRI, can accurately exclude lymph node metastases in clinically node negative patients, making SLND a redundant operation in node negative patients. Consequently, node negative patients would no longer harm from axillary surgery. In addition, cost-effectiveness of implementation of dedicated axillary hybrid PET/MRI should also be investigated.

Since the introduction a few years ago, hybrid PET/MRI has been incorporated in daily clinical practice for several (neurologic) indications. So far, no research has been performed investigating the feasibility of dedicated axillary hybrid PET/MRI to improve lymph node staging in breast cancer. This thesis demonstrated that dedicated axillary hybrid PET/MRI for lymph node staging is

feasible and it changed nodal status when compared to current imaging modalities.

Besides, diagnostic performance of dedicated axillary hybrid PET/MRI after neoadjuvant systemic therapy in clinically node positive patients should be investigated to determine whether this technique can accurately identify axillary pCR. This would allow patients who converted to axillary pCR to omit any further axillary surgery, which would be even more beneficial compared to RISAS-procedure.