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Simultaneous use of an ^{125}I-seed to guide tumour excision and ^{99m}Tc-nanocolloid for sentinel node biopsy in non-palpable breast-conserving surgery

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Abstract

Purpose: In the present study we describe patients with non-palpable breast lesions, in which an Iodine-125 (^{125}I)-marker (or "seed") for excision of the primary tumour and Technetium-99m nanocolloid (^{99m}Tc-nanocolloid) for sentinel node biopsy (SNB) are used simultaneously. The purpose was to investigate any interference between ^{125}I-seeds and ^{99m}Tc-nanocolloid by an *in vitro* and *in vivo* analysis.
Methods: Contrast/interference-ratios between ^{125}I and ^{99m}Tc count-rates were determined *in vitro* using a realistic simulation model. Measurements were performed with 3 gamma-probes with different crystal materials. In 25 consecutive patients ^{99m}Tc-nanocolloid was intratumourally administered at the site of a previously implanted ^{125}I-seed. Respectively, the ^{125}I-setting and ^{99m}Tc-setting of the gamma-probe guided the wide local excision and SNB and maximum counts-per-second (cps) were measured.
Results: *In vitro* the different probes varied in ^{125}I- and ^{99m}Tc-sensitivity. The contrast-ratio between ^{125}I and ^{99m}Tc in the ^{125}I-channel was 4.6 for a 3-month-old ^{125}I-seed using the most appropriate gamma-probe. *In vivo* the gamma-probe in the ^{125}I-setting measured a median of 16,300 cps at the tumour site compared to 4820 cps using the ^{99m}Tc-setting. The ^{125}I-seed could be well distinguished from the ^{99m}Tc-nanocolloid in 92% of the patients and 96% required a single operation. The SNB was successful in all patients.
Conclusions: Simultaneous use of ^{125}I-seeds and ^{99m}Tc-nanocolloid is possible under well-standardised conditions. Non-palpable breast lesions can be safely excised using the ^{125}I-seed in combination with a SN procedure. Use of ^{125}I-seeds is a next step within fine-tuning breast-conserving surgery that should lead to further investigation to confirm its value.

Keywords: Breast cancer; Breast conserving surgery; Non-palpable; Sentinel node procedure; Iodine 125; Technetium 99m

Introduction

The challenge of nowadays widely performed breast-conserving surgery is to achieve tumour-free margins while excising no more breast tissue than necessary. An incomplete resection is a risk factor for local recurrence and mortality and should be avoided whenever possible.[1–3] This issue

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especially concerns excising non-palpable breast lesions where the surgeon is dependable on a localisation technique.

Different localisation techniques are being used. Wire localisation is one of the first used guiding methods.[4] The wire, if inserted correctly, should indicate the centre of the lesion, and consequently does not point out the margins of the tumour. Unfortunately, dislocation of the wire has been often described. Radioguided occult lesion localisation (ROLL), the ROLL-technique, is another popular technique[5–7] based on the injection of Technetium-99m albumin macro-aggregates for allocation of the breast lesion. Technetium-99m-nanocolloid (^{99m}Tc-nanocolloid) is injected into the centre of the tumour to visualise both the lymphatic drainage and localise the breast lesion (Sentinel Node and Occult Lesion Localisation (SNOLL)).[8] Both the wide local excision and the sentinel node biopsy (SNB) are guided by a handheld gamma-probe. The accuracy of injecting the radiopharmaceutical in the middle of the lesion determines its success. The radioactive depot at the tumour-site often exceeds the amount of tissue necessary to remove.

Ultrasound can also guide the breast lesion excision.[9,10] Unfortunately, not all non-palpable lesions, especially DCIS, are visible on ultrasound.[10]

Radioactive seed localisation (RSL) is an alternative localisation method to the techniques mentioned above.[11–14] An Iodine-125 (^{125}I) seed is preoperatively implanted in the centre of the lesion and during the operation the gamma-probe guides the local excision using the ^{125}I-setting. This technique has some of the same limitations as the ROLL-technique. The seed has to be placed correctly and there is, also, a lack of indication of the lesion margins. However, the seed is a focused point source and does not diffuse into its surrounding. This enables the conservation of healthier breast tissue. Moreover, ^{125}I-seeds are radiographically detectable and one always knows the exact placement of the seed in relation to the tumour by using routinely performed mammography[15] (Fig. 1).

However, the simultaneous use of RSL for tumour excision and ^{99m}Tc-nanocolloid for SNB has not yet been published and for this purpose it is essential to know to what extent the radioactive ^{99m}Tc-labelled radiopharmaceutical depot interferes with the activity emitted by the ^{125}I-seed. It is known that scattered radiation from ^{99m}Tc (peak 140 KeV) will be detected in the energy-window of ^{125}I (peak 30 keV). This is due to the Compton effect where photons scatter in the breast tissue and turn in to photons with lower energy contents.[16]

In the present study variable ^{125}I-activities, tracer protocols, and 3 gamma-probes are evaluated in an *in vitro* study to analyse the interference between the two isotopes, and thereby, to make sure the tumour is excised based on the activity of the seed and not by the depot of ^{99m}Tc-nanocolloid. Hereafter, this topic is described in patients with non-palpable breast lesions in which both an ^{125}I-seed and an injection of ^{99m}Tc-nanocolloid are placed in the centre of the lesion for combined RSL and SNB.

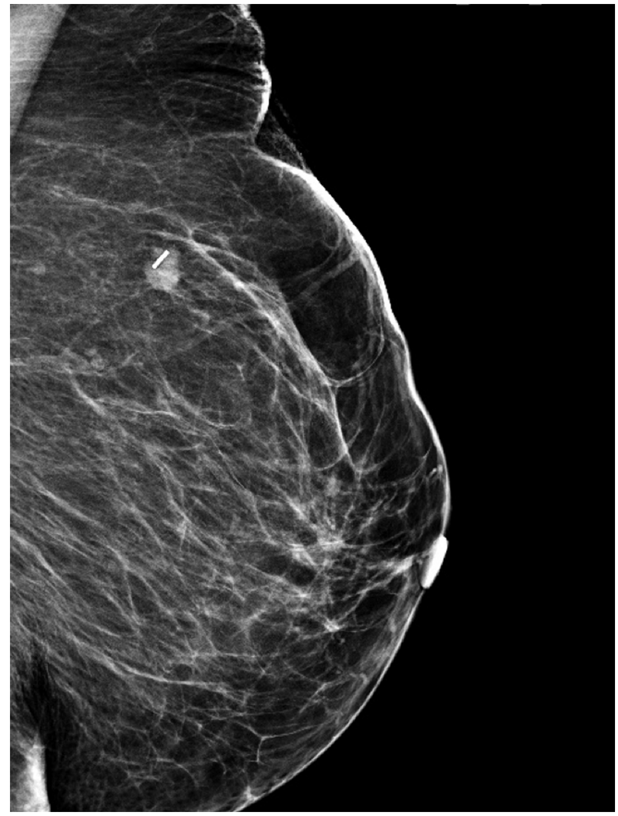

Figure 1. Mammogram with an implanted ^{125}I-seed.

Methods

In vitro study

The *in vitro* experiments were conducted to study the sensitivity and distinctive capacity between ^{125}I and ^{99m}Tc. Three gamma-probes (A, B, and C)[f] were compared based on sensitivity for ^{125}I and ^{99m}Tc. Contrast-ratios in the ^{125}I-setting between ^{125}I and ^{99m}Tc (formula: ^{125}I-cps/^{99m}Tc-cps) at a 2 cm simulated lesion depth were determined. In our institute a two-day protocol is used for SNB, on the first day maximal 140 MBq ^{99m}Tc-nanocolloid is intratumourally administered.[17] The combination of RSL with SNB was simulated with an ^{125}I-seed of 3 months old (2.9 MBq) together with approximately 8 MBq ^{99m}Tc, taking only the physical decay of ^{99m}Tc in a two-day protocol into account.

Gamma-probe A is equipped with a Cadmium Zinc Telluride crystal. The wireless Bluetooth probe was not suitable to specifically measure ^{125}I in a combined RSL-SNB procedure; as it measures a window with the lower

[f] A is the Neoprobe® (Johnson & Johnson Medical B.V., Hamburg, Germany), B is the Crystal probe (Crystal Photonics GmbH, Berlin, Germany), and C is the Node Seeker (Intramedical Imaging Llc Hawthorne, Canada). The Neoprobe and wired probe were used for the *in vivo* experiments.