MeMaLoc: Magnetic Marker Localization for Melanoma Surgery. A feasibility study.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON42850

Source
ToetsingOnline

Brief title
MeMaLoc-1

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified
- Skin neoplasms malignant and unspecified
- Skin and subcutaneous tissue therapeutic procedures

Synonym
melanoma, skin cancer

Research involving
Human

Sponsors and support

Primary sponsor: Nederlands Kanker Instituut
Source(s) of monetary or material Support: Ministerie van OC&W,STW Take-off Fase 1

Intervention

Keyword: Localization, Melanoma, Non-palpable, Surgery

Outcome measures

Primary outcome

1. Retrieval rate: in how many cases is the surgeon able to adequately localise

and remove the marked lesion using the magnetic detection technology.

Secondary outcome

2. Radiologist satisfaction: to what extent is placing the experimental

magnetic marker comparable to the current clinical practice, what is different

and what are (dis)advantages?

3. Surgeon satisfaction: how does intraoperative localisation using the

magnetic technology compare to the current clinical practice, what is different

and what are (dis)advantages?

Study description

Background summary

Since the 1990s, the incidence of melanoma has nearly quadrupled], and although it occurs fewer than other skin cancer types, it is the most deadly type with approximately 10.000 annual deaths in the USA alone.

Melanoma diagnosis is based upon diagnostic excision of the area of interest, in the Netherlands usually performed by a general practitioner. If the pathology analysis turns out to be melanoma, surgery is the cornerstone of further treatment. A surgeon will perform a wide local excision (WLE) of the area, combined with sentinel lymph node biopsy (SLNB) for tumours with a

Breslow thickness larger than one millimetre, to assess lymphatic involvement. In the case of involved lymph nodes, an additional Complete Lymph Node Dissection (CLND) of the involved area is indicated.

Unfortunately, melanoma is prone to recur in 19% of patients. Recurrence may be 1) local (* 3cm of primary lesion); 2) in-transit (anywhere in the lymphatic trajectory between the site of the primary lesion and the nearest connected lymph node); 3) Regional (in the nearest lymph nodes) and 4) distant. It is important to recognize that *recurrent* lesions may occur concurrently with diagnosis of the primary lesion.

IN TRANSIT AND DISTANT METASTASES
Of these recurrences, in-transit metastases (ITMs) occur in approximately 4-8% of all melanoma cases. These rates are considerably higher for SLNB-positive cases, at approximately 22%. ITMs have large implications for survival. Patients with ITMs have a 5-year survival rate ranging from 46% to 59%, as opposed to for example local recurrences (74%). In a surgical curative approach, removing all ITMs with a relevant margin is essential to maximize chances at survival.

Distant metastases occur in 14% of cases, and have even bigger implications for survival. Only 30% of patients with distant metastases are alive five years after diagnosis. Increasingly, our surgeons are faced with the request to remove leftover distant subcutaneous or muscular metastases of stage IV cancer after successful systemic therapy (e.g. immunotherapy or targeted therapy) to improve prognosis.

Unfortunately, localizing these recurrences during surgery can be very challenging, especially in limbs that are severely affected by lymphedema after CLND, making the lesions essentially non-visible and non-palpable (or clinically occult). In current clinical practice, a radiologist is required to assist in this matter: pre-operative localization of occult lesions is performed using ultrasound (US), and the approximate locations are marked on the skin with a pen. In correspondence with our melanoma surgeons, it was hypothesized that more accurate localization of these recurrences is expected to lead to more successful surgeries, narrower margins or * at the least * more confidence of optimal surgical treatment.

The rudimentary type of localization applied for these melanoma recurrences contrasts sharply with localization procedures in breast cancer care. There, both primary and recurrent occult lesions as well as sentinel lymph nodes are marked using radioactive iodine seeds for accurate intra-operative localization using a gammaprobe. There are several case reports in which this Radioactive Seed Localization (RSL) approach was applied for surgical treatment of for example ITMs, however due to legislative and certification challenges there is currently no expectation of this technology becoming clinical practice in the (near) future.

MARI PROCEDURE
As stated above, marking the axillary lymph node with radioactive iodine seeds (MARI procedure) has recently been tested as a feasible technology in breast cancer patients that are treated with neoadjuvant systematic therapy. The technology allows axilla-conserving surgery in patients responding well to neoadjuvant therapy.

Unfortunately, the use of radioactive seeds for this purpose is stated to *require authorization by the government and safety issues need to be addressed*. This fact is inherent to using radioactive iodine seeds for localization and most notably it is the reason for the relatively poor uptake of radioactive seed localization for breast conserving surgery. This fact, combined with the limited availability of radioactive substances in the western world * reported as low as 60% * and the European Commission that urges the development of non-radioactive alternatives to current radioactive technologies warrants the scientific exploration of feasible alternatives.

THE MAMALOC TECHNOLOGY
Recently, our research group has developed and tested a novel method for localization of primary breast lesions. In this method, a magnetic marker (or magnetic seed) is used in combination with a magnetic detection platform during surgery to reach essentially the same goal as Radioactive Seed Localisation (RSL): accurate intra-operative localization of a tissue of interest. The technology was named MaMaLoc (Magnetic Marker Localization).

By using the physical principle of magnetism for localization rather than radioactivity, the clinical applicability of the MaMaLoc technology is hypothesized to be much larger. There is little to no legislation or regulation involved as magnetism is inherently safe. In a first safety and feasibility trial in this institute (MaMaLoc-1, N15MML, data yet unpublished) the technology was applied successfully, without marker migration and without adverse events in 15 patients for non-palpable breast tumour localization.

After this successful application, we are now interested in obtaining proof-of-principle of the technology for additional clinical indications. As stated, the challenge of surgical localization is at times just as apparent in surgery for melanoma metastases as it is in breast surgery, however the application of iodine seeds for this type of surgery is not possible due to certification issues with the iodine seeds. Second, the possibility to mark, detect and remove a suspect lymph node using our technology would open the door for a future in which high-morbidity and unnecessary CLNDs may become history, without compromising patient survival. In addition, the possibility of accurately localizing and removing a marked lymph node has implications for all lymphogenetically metastasizing tumour types.

Study objective

Concluding, the aim of current study is to show feasibility of the MaMaLoc technology for surgical localization of clinically occult melanoma lesions, as well as to show feasibility of the MaMaLoc technology for lymph node detection, both in the axilla and inguinal region.

Study design

Non-controlled, non-blinded, non-randomized interventional study to assess feasibility of a novel intraoperative localisation technology (MaMaLoc) for patients with a history of melanoma.

Intervention

Subjects will receive an ultrasound-guided placement of a magnetic marker (the MaMaLoc marker) in a lesion that will be later removed during surgery. This is either a locoregional or distal non-palpable ((sub)cutaneous or muscular) metastasis (Group 1) or a (suspect) lymph node in an area that is to be removed during a complete lymf node dissection of the axillar or inguinal region.

Study burden and risks

Burden is limited to one extra visit to the radiology department for echoguided placement of the marker, this also means one extra injection. This takes approximately 15 minutes. Ideally, this appointment is planned at the same day as another appointment at the hospital to avoid extra travelling. For patient enrolled in group 2, surgery may last an additional 5-10 minutes.

Risk is low. The technology has been successfully applied in 15 patients with breast cancer (no adverse events, no marker migration). The areas that are marked need to be removed anyhow and there is no adjustment of the clinical practice.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. 18 years or older
2. Signed informed consent
3. Scheduled for either
* Surgery of clinically occult (sub)cutaneous or muscular melanoma lesion(s) (group 1)
OR
* Complete Lymph Node Dissection of inguinal or axillary region (group 2)

Exclusion criteria

- MRI necessary in period between placement of magnetic marker and surgery

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2016
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Generic name:	MaMaLoc (Magnetic Marker Localisation)
Registration:	No

Ethics review

Approved WMO

Date:	24-11-2016
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL58293.031.16