Superparamagnetic iron oxide-enhanced magnetic resonance imaging for sentinel lymph node identification in oral cancer: a feasibility study

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To explore the feasibility of sentinel lymph node identification by SPIO injection followed by MRI in head-and-neck cancer patients.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Observational invasive

Summary

ID

NL-OMON51046

Source
ToetsingOnline

Brief title
MAG-NODE study

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
oral cancer, Oral cavity carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Magnetic resonance imaging, Oral cancer, Sentinel lymph node identification, Superparamagnetic iron oxide (SPIO)

Outcome measures

Primary outcome

Feasibility of SPIO-enhanced MRI for SN detection in oral cancer patients:

- To optimize dose of SPIO injection

- To optimize the timing of MRI

- To assess whether SNs detected by conventional 99mTC-nanocollloid injection

and SPECT-CT are concordant with those visualized by SPIO injection and MRI

Secondary outcome

- To assess the distribution of SPIO within a lymph node by comparing in vivo

MR-images and histopathological staining

Study description

Background summary

Head-and-neck cancer (HNC) mostly comprises tumors in the oral cavity, pharynx & larynx. Worldwide, HNC accounts for more than 650.000 cases annually. The main treatment modalities are surgery and radiotherapy. Despite modern imaging methods, up to 30% of HNC patients with a clinically and radiologically negative neck (cN0) appear to have metastases. Therefore, elective radiotherapy target volume in HNC includes the whole neck, often bilaterally. This results in overtreatment of at least 70% of patients. Since the elective target is in close proximity to critical anatomical structures (e.g. salivary glands, swallowing muscles, thyroid gland and large blood vessels), the effect of treatment has a negative impact on the quality-of-life in HNC survivors.
The presence of lymph node metastases has a large impact on prognosis and necessitates either intensification of radiotherapy or extended surgery. Therefore, tailoring HNC treatment to individual patients requires an accurate pretreatment assessment of the nodal status. The sentinel lymph node biopsy (SNB) is current standard-of-care in oral cavity cancer and comprises

peritumoral 99mTc radioisotope injection followed by single photon emission computed tomography (SPECT) for SN localization and surgical resection. The procedure aims to identify the first echelon of draining lymph nodes, which are resected and evaluated for metastatic disease. SNB is a reliable method for staging the cN0 neck in oral cancer and identifying patients with small nodal metastatic disease, but requires an invasive procedure including the use of radioactive tracer.
Peritumoral injections of superparamagnetic iron oxide (SPIO) nanoparticles hold promise as non-radioactive tracer to accurately detect sentinel lymph nodes. After injection, the particles are drained via the lymphatic system and become trapped in the SN(s). As a result of its paramagnetic properties, SPIO generates a negative enhancement in T2*-weighted iron sensitive multi gradient echo (MGRE) magnetic resonance imaging (MRI) sequences. Moreover, evaluation of 102 consecutive breast cancer patients who underwent SPIO-enhanced MRI for SLN detection showed its capability in accurately staging the axillary SNs. Assessment of lymph node status on a nodal basis showed a sensitivity, specificity, NPV and PPV of 81.5, 90, 94.2, and 71%, respectively. A subsequent study evaluating the pattern of SPIO uptake in 33 positive SLNs obtained from 30 breast cancer patients showed that in lymph nodes containing metastases of >2 mm, the area of high signal intensity on SPIO-enhanced MRI correlated with the size of metastases identified by pathology. These early results indicate that SPIO-enhanced MRI is capable of minimally invasive SN assessment.

Study objective

To explore the feasibility of sentinel lymph node identification by SPIO injection followed by MRI in head-and-neck cancer patients.

Study design

Single center feasibility study.

Study burden and risks

- Possible side-effects are predominantly hypersensitivity reactions following subcutaneous SPIO administration. If injection appears to be painful, local anesthetics will be used. Since we intend to use a very low dosage of SPIO we expect a minimal risk of side-effects.
- Results of a recent trial in breast cancer from our colleagues from the university of Twente show residual SPIO particles at the injection site after an interval of approximately five years after administration in breast cancer patients (unpublished data). Although considered harmless, these particles may lead to (very small) artifacts on subsequent MRI-scans. The dose used in this trial was substantially higher compared to the dose we intend to use. For this reason we believe that this burden of residual SPIO is minimal.
- One MRI-scan which takes approximately 30 minutes and causes some discomfort.

- There is a low risk of unexpected findings.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female aged >18 years.
- Patients with histopathologically proven cT1-2N0M0 squamous cell carcinoma of the oral cavity.
- Patients planned to undergo routine sentinel node biopsy with 99mTc-radioisotope and SPECT-CT.
- Patient provided written informed consent.

Exclusion criteria

Patients who underwent previous surgery or radiotherapy to the neck.

Contra-indications to SPIO:
- prior allergic reaction to SPIO or any other iron preparation
- prior allergic reaction contributed to dextran or other polysaccharide, in any preparation
- prior allergic reaction to contrast media of anytype
- hereditary hemochromatosis, thalassemia, sickle cell anemia

Patients unable to provide informed consent.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-07-2021
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Magtrace(r)
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	11-05-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL77078.091.21