Multispectral optoacoustic imaging using cetuximab-800CW for detection of cervical lymph node metastases: a single center proof of concept study

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The main objectives of this study is to evaluate if EGFR positive cervical lymph node metastasis can be detected non-invasively using the MSOT Acuity Echo with cetuximab-800CW as contrast agent in patients with oral squamous cell carcinoma.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metastases
Study type	Observational non invasive

Summary

ID

NL-OMON48019

Source
ToetsingOnline

Brief title
OPUS

Condition

- Metastases

Synonym
cervical lymp node metastasis, cervical metastasis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: EGFR, Lymph node metastasis, Optoacoustic

Outcome measures

Primary outcome

Quantification of the cetuximab-800CW optoacoustic signal and the tracer distribution observed by multispectral optoacoustic imaging using the MSOT Acuity Echo in vivo in patients with oral squamous cell carcinoma.

Secondary outcome

- Correlation between optoacoustic signal and fluorescence intensity of cetuximab-800CW in cervical lymph nodes.

- Standard histopathological assessment (i.e. hematoxylin and eosin staining) to correlate optoacoustic signal detected in vivo with histology using surgical specimens;

- Histopathologic characteristics of surgical specimens related to EGFR-status and tracer distribution.

Study description

Background summary

The presence of lymph node metastasis is one of the most important prognostic factors in oral squamous cell carcinoma (OSCC). In addition, it is an important factor in determining the appropriate treatment plan in patients with OSCC. However, detection of lymph node metastases by means of current imaging modalities is limited. 20-30% of patients with a clinically negative neck (cN0) harbour lymph node metastasis that were not detected during clinical diagnostic workup, which are referred to as occult lymph node metastasis. Personalized management of the neck would benefit greatly from staging techniques that

increase the accuracy of the assessment of nodal disease. In addition, visualizing the pattern of lymphatic spread can possibly lead to more targeted neck dissections and thereby reduce morbidity. Clearly, there is need for additional diagnostic tools in order to identify lymph node metastasis and thereby support the decision making for treatment of the neck.
Optoacoustic imaging is a novel imaging method in which an ultrashort laser pulse is used to irradiate biological tissue. Consequently, optoacoustic or photoacoustic waves are generated which can be measured by wideband ultrasonic transducers. Optoacoustic imaging has been shown to address clinically relevant aspects of various cancers. It also enables the visualization of targeted tumor-specific biomarkers by detecting optoacoustic waves. We hypothesize that accumulation of cetuximab-IRDye800CW can be detected in lymph node metastasis, enabling better visualization of regional metastatic disease compared to current imaging modalities. We believe that this approach can improve detection of lymph node metastases and thereby supports decision making for treatment of the neck.

Study objective

The main objectives of this study is to evaluate if EGFR positive cervical lymph node metastasis can be detected non-invasively using the MSOT Acuity Echo with cetuximab-800CW as contrast agent in patients with oral squamous cell carcinoma.

Study design

The current study is a single center, prospective, cross-sectional, proof of concept study. The study will be carried out by the out at the University Medical Center Groningen, Department of Oral and Maxillofacial Surgery and Department of Nuclear Medicine and Molecular Imaging. Further analysis of sections of the lymph node metastasis will be done at the Department of Pathology.

Study burden and risks

Burden
- Time investment: Patients need to visit the UMCG two to four days before their planned surgery according to the ICON-study which will take approximately 2 hours. For the imaging that will be performed prior to tracer administration (part of the ICON study), additional 20-30 minutes are necessary. Usually patients are admitted one day prior to surgery. Therefore the imaging on this day will not require extra time investment
- Extra procedures: Two imaging procedures, prior to tracer administration and on day of admission.

Risks

The optoacoustic imaging device uses a class IV laser and therefore is a risk for cornea and skin. Several measurements described below, are taken to reduce the risk of injuries to an absolute minimum.

Benefit
Patients will have no direct benefit from this study.

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

In order to be eligible to participate in this study, the subject must meet the inclusion criteria of the ICON study (NCT03134846), which are as follows:
1. Biopsy confirmed diagnosis of primary or recurrent HSCC and scheduled to undergo surgical resection as decided by the Multi-Disciplinary Head & Neck Tumor Board of the

UMCG.
2. Age * 18 years
3. Written informed consent
4. Adequate potential for follow up
5. Acceptable hematologic status, kidney function, and liver function, as standard surgery protocol requires.

Exclusion criteria

Patients will be excluded when they meet one of the exclusion criteria of the ICON study (NCT03134846), which are as follows:
1. Medical or psychiatric conditions that compromise the patient*s ability to give informed consent;
2. Concurrent uncontrolled medical conditions;
3. Received an investigational drug within 30 days prior to the dose of cetuximab-IRDye800CW;
4. Tumors at sites of which the surgeon would assess that in vivo imaging would not be feasible;
5. Had within 6 months prior to enrollment: myocardial infarction, cerebrovascular accident, uncontrolled cardiac heart failure, significant liver disease, unstable angina
6. Inadequately controlled hypertension with or without current antihypertensive medications;
7. History of infusion reactions to cetuximab or other monoclonal antibody therapies
8. Pregnant or lactating women. Documentation of a negative pregnancy test must be available for women of childbearing potential. Woman of childbearing potential are premenopausal women with intact reproductive organs and women less than two years after menopause;
9. Evidence of QT prolongation on pretreatment ECG (greater than 440 ms in males or greater than 450 ms in females);
10. Lab values that in the opinion of the primary surgeon would prevent surgical resection;
11. Patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents;
12. Magnesium, potassium and calcium deviations that might lead to cardiac rhythm (grade II or higher deviations by CTCAE);
13. Life expectancy < 12 weeks;
14. Karnofsky performance status < 70%.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	MSOT Acuity Echo
Registration:	No

Ethics review

Approved WMO

Date:	28-03-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL67343.042.18