Combination of salvage surgery and adjuvant photodynamic therapy in management of recurrent or residual sinonasal tumors.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON43342

Source
ToetsingOnline

Brief title
Adjuvant PDT to surgery in recurrent or residual sinonasal tumors.

Condition

- Miscellaneous and site unspecified neoplasms benign
- Head and neck therapeutic procedures

Synonym
paranasal malignancies / mid-face tumors

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: irradical surgery, photodynamic therapy, salvage surgery, sinonasal tumors

Outcome measures

Primary outcome

The main study parameter is to guarantee the delivery of a homogeneous light dose of around 20 ± 5 joule/cm2 at the target region by developing, validating and clinically evaluating an accurate and specific treatment method making use of dosimetry and spectroscopy measurements. Translational research including augmented 3D endoscope imaging, haptic feedback and a mechatronic support aid will be explicitly tested ex vivo and in vivo on feasibility, safety and usage.

Secondary outcome

The secondary study parameter is to evaluate the safety and tolerability of PDT of the paranasal sinuses by monitoring the adverse side effects such as prolonged systemic photosensitivity, infections etc. according to the common terminology criteria for adverse events v4.0 (CTCAE). No major complications of CTCAE grade 5 and nog more than 20% grade 3-4 complications will be considered as positive result. The preliminary study did not show a grade 5 toxicity, therefore we expect no grade 5 toxicity in this study.

Effectiveness will be evaluated using recurrence-free survival and recurrence-free survival analysis. Local tumor control will be measured at 3

and 6 months after treatment by MRI or CT. Changes within patient*s quality of

life will be objectified using European Organization for Research and Treatment

of Cancer (EORTC) questionnaires.

Study description

Background summary

Malignant tumors of the paranasal sinuses and anterior skull base recur frequently after surgery and radiotherapy. The management of these recurrent tumors remains a major challenge. The vicinity of essential structures limits additional treatment options, such as radical surgery and re-irradiation. There is a serious demand for an effective minimally invasive local approach. Photodynamic therapy (PDT) can be a feasible adjuvant treatment option to salvage surgery in treatment of recurrent sinonasal tumors. Meta-tetrahydrophenylchlorine (m-THPC) mediated PDT is shown to be effective in head and neck tumors. The patient is intravenously administered with a photosensitizer, and activated by light using a fiber-optic source. This leads to a photochemical reaction resulting in tumor cell death. A preliminary study (n=15) of PDT as adjuvant therapy to surgery of the paranasal sinuses, conducted in our institute showed promising results in safety and clinical response. The current technique is removal of the tumor as much as possible, and apply PDT to the resulting cavity with only visual feedback i.e., observing in the endoscopic image where red treatment light illuminates.

During the preliminary study the PDT implementation showed some shortcomings namely;
a) Absence of a treatment planning strategy.
b) Non-standardized treatment approach.
c) Substantial variations in light dose due to hand-held source positioning.
d) No feedback on the actual source location.
These shortcomings lead to failure to deliver the effective light dose of 20 Joule/cm2.

The chance of achieving a homogeneous light distribution of exactly 20 joule/cm2 in a complex geometry with varying optical properties (color) such as the maxillary sinuses is improbable. The observed intra patient variations range from 5 up to 40 joule/cm2. Our hypothesis is that an accurate PDT light distribution planning strategy in combination with EM navigation guided source positioning, will increase the homogeneity up to 20 joule/cm2 ± 5. We thereby avoid regions over- and underexposure more effectively.

Study objective

The main objective of this study is to develop a PDT and salvage surgery combination specific for recurrent or residual tumors of the sinonasal cavities, unsuitable for the conventional treatments like radical surgery or radiotherapy with curative intent. With the delivery of a therapeutically effective, homogeneous light dose to the complex and irregular geometry of the paranasal sinuses.
Development of an accurate treatment method will be done by:
a) 3D CT/MR fused pre-treatment planning to find the optimal source locations (OSLs).
b) Standardized light exposure based on the planned OSLs, source parameters, and verified by in vivo dosimetry and spectroscopy measurements.
c) Quantitative and accurate navigation of the source towards the OSLs.
d) Stable fixed positioning of the source at the OSL.

Additional objectives are to evaluate the safety and effectiveness of this standardized treatment method.

Study design

The proposed study is a longitudinal study that will be conducted on patients with recurrent or residual tumors of the sinonasal cavities without curative treatment options. The patients will undergo open or endoscopic salvage surgery to remove the macroscopic tumor or debulk the tumor as much as possible. An MRI/CT obtained after surgery will be used to develop a pre-PDT treatment plan including the number, locations, types of light sources and light dose to be used. 4-6 weeks after salvage surgery PDT treatment will be performed. During the PDT treatment non-invasive (fluorescence) spectroscopy and light dosimetry measurements will be done to gain information about the light distribution, the tissue optical properties and pharmacokinetics of the photosensitizer. Neuronavigation will be used to guide the source device to the OSL. As the second phase, translational research will be carried out including navigation combined with augmented 3D endoscopic imaging and haptic feedback to guide the source device to the OSL and fixation by custom made mechatronic support in order to provide source stability. Follow-up will consist of an MRI 3 and 6 months after PDT. This treatment will be performed in two Dutch Head and Neck Oncology Centers; the Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL) and the Erasmus Medical Center (EMC). Design of technical interventions will be performed at the University of Twente (UT).

Intervention

PDT treatment after salvage surgery.

Study burden and risks

The experimental nature of the treatment will be discussed in detail with the patient. The burden is high, because the patient has to undergo a salvage operation and PDT treatment, which means that they have to go under general anesthesia twice. PDT is associated with systemic light sensitivity for a period of 2-3 weeks. The patients will receive counselling and written information about light avoidance measures. There is already a running PDT program in house where all the counseling is routinely given. No other risks are associated with participation to this study in comparison with the current salvage surgery methods and PDT treatment of malignancies of the paranasal sinus. The patients do not have to visit the hospital extra. Patients will have to fill in quality of life questionnaires at four different time points. The burden is high; however there are no other suitable treatment options for these recurrent malignancies.

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

1. Eligibility reviewed and approved by an interdisciplinary hospital team.
2. Age >= 18 years.
3. Histopathological or cytological confirmed diagnosis of recurrent or residual tumor of the sinonasal cavity, maxillary sinus or anterior skull base, considered unsuitable for radical surgery or radiotherapy with curative intent. Patients with distant or regional metastatic disease may be eligible if local palliation is needed.
4. Performance status according to the Eastern Cooperative Oncology Group (ECOG) performance scale <= 3
5. Eligibility to undergo general anesthesia.
6. Written informed consent.

Exclusion criteria

1. Other concurrent anticancer therapies.
2. Current or recent (within 30 days of first study treatment) participation in another investigational study.
3. Treatment with a medicinal product with known or potential drug-drug interaction with m-THPC.
4. Conditions that worsen when exposed to light (including porphyria).
5. Inability to undergo CT or MR imaging.
6. Pregnancy or lactation (female patients with childbearing potential). A serum pregnancy test has to be performed within 7 days prior to study treatment start.
7. Known allergy or sensitivity to photosensitizers.
8. Ataxia telangiectasia.
9. Evidence of any other medical conditions (such as psychiatric illness, infectious diseases, physical examination or laboratory findings) that may interfere with the planned PDT treatment, affect patient compliance or place the patient at high risk from treatment-related complications.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-07-2017
Enrollment:	0
Type:	Actual

Ethics review

Approved WMO

Date:	13-01-2017
Application type:	First submission
Review commission:	METC NedMec

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	NL58084.031.16