Defining optimal imaging strategies for diagnosis, treatment, and treatment evaluation of chordomas and chondrosarcomas of the axial skeleton

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Show that functional MR tumor plasma volume parameters Vp,max and Vp,mean change significantly within 1-6months following start of proton beam radiotherapy of chordoma.

Ethical review	Approved WMO
Status	Pending
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON54229

Source
ToetsingOnline

Brief title
Optimization of chordoma and chondrosarcoma proton therapy

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
Bone tumor

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Varian Medical Systems

Intervention

Keyword: Chondrosarcoma, Chordoma, MR imaging, Proton therapy

Outcome measures

Primary outcome

Primary parameters are MRI mean and max tumor plasma volumes Vp.

Secondary outcome

Secondary parameters are MRI perfusion AUC time-intensity curves, slopes, T1

mapping, volumetric analysis,

cellularity-mean ADC, Min ADC, Max ADC, permeability Ktrans, Kep, Kel, AUC.

Evaluation of the soft tissue target

volume will be correlated to quality of life parameters (function of cerebral

nerves near skull base, lumbar and sacral

roots in the sacrum). Following PET-CT parameters: SUVmax [g*mL-1], SUVpeak

[g*mL-1], SUVmean [g*mL-1], MTV [ml], TLG [g], texture features parameters,

along with progression free and disease specific survival.

In patients who are treated with surgical resection following neo-adjuvant

therapy, the surgical specimen will be

correlated with imaging findings.

Study description

Background summary

Chordomas and chondrosarcomas located in the axial skeleton are malignant neoplasms of bone. These tumors share
the same clinical challenges, as the effect of the disease is more a function of their local aggressiveness than their

tendency to metastasize (20% metastasize). The local aggressive behavior can cause debilitating morbidity and
mortality by destruction of nearby located critical neurovascular structures. Imaging has, in addition to histopathology,
a role in diagnosis and in guiding (neo)adjuvant and definitive treatment. Despite the low sensitivity to radiotherapy,
proton radiotherapy has been successfully used as an adjunct to resection or as definitive treatment for aggressive
chordomas and chondrosarcomas, making it a standard indication for proton therapy in the Netherlands.
Chordomas and chondrosarcomas consist, especially after previous therapy, of non-viable and viable tumor
components. Identification of these viable components by functional imaging is important to determine the effect of
previous therapy, as change in total tumor volume occurs more than 200 days after change of functional imaging
parameters. [1] Study hypothesis is that these viable tumor nodules detected with functional imaging can be used to
direct proton therapy, which is characterized by its accurate target volume, in the future.

[1] Santos P, Peck KK, Arevalo-Perez J, Karimi S, Lis E, Yamada Y, Holodny AI, Lyo J, T1-Weighted Dynamic
Contrast-Enhanced MR Perfusion Imaging Characterizes Tumor Response to Radiation Therapy in Chordoma, http://
dx.doi.org/10.3174/ajnr.A5383

Study objective

Show that functional MR tumor plasma volume parameters Vp,max and Vp,mean change significantly within 1-6
months following start of proton beam radiotherapy of chordoma.

Study design

The design of this study is a prospective cohort study.

Study burden and risks

Extra MRI and PET-CT examinations will be planned during proton therapy. As this extra imaging is performed in
HollandPTC during treatment there will be no additional burden on patient regarding mobility. However, additional
scanning might represent an additional burden to the patient as he/she will

receive extra dose (see Appendix A) and
the scanning procedure will add up to 3 extra hours spent at the HollandPTC compared to the standard protocol.

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, a subject must meet all of the following criteria: referred to HPTC, or LUMC, or the Netherlands Committee of Bone tumors, histologically diagnosed with primary or recurrent chordoma or chondrosarcoma in the axial skeleton (clivus, spine and sacrum), and accepted for standard proton beam therapy.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Diagnosis other than chordoma or chondrosarcoma is made.
- Patient refuses (parts) of the standard treatment protocol.
- Patient refuses MRI due to claustrophobia.
- Patient not suitable for MRI due to the presence of MRI incompatible implants.
- Incapacitated patients.
- Patient doesn*t allow coded data to be used for analysis.
- Patient is under 18 years of age.
- Lesion size less than 1cm.
- Patients with WHO 3 and higher.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-03-2021
Enrollment:	40
Type:	Anticipated

Ethics review

Approved WMO

Date:	02-02-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	12-07-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	23-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	27-03-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
ClinicalTrials.gov	NCT04832620

Register
CCMO

ID
NL73476.058.20