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Project description (5 pages, in English)

The project description should include: background, hypotheses, materials and methods, research plan, perspectives and should clearly state the applicant's part in the research.

Academic title and name: MSc in Physics, Peter Georgi
Project title: Enhancing the Utilisation of In Vivo Dosimetry for Low-Energy Radiotherapy

Project description 12000 exclusive reference (11995)

AIM

The overall aim of this project is to develop and test easily accessible online treatment verification (OTV) systems for brachytherapy (BT) and electronic BT (eBT) paving the way for improved quality assurance in these modalities.

BACKGROUND

Brachytherapy

BT is a radiotherapy modality in which cancer is treated with short ranged radiation obtained via low-energy sources. This leads to steep dose fall offs, which ensures focal dose delivery that spares adjacent organs at risk.
At Aarhus University Hospital (AUH) BT is used to treat cervical, prostate, rectal, and skin cancer. For the first two radioactive sources are placed inside or close to the tumour. The two latter are treated with low-energy X-rays produced from stopped electrons, i.e. electronic BT (eBT).
BT has a good clinical outcome [1,2], but the quality is challenged by two key components. The steep dose gradients demand high geometric accuracy. A few millimetres offset can lead to large over or under dosages of tumour and normal tissue. Furthermore, the procedure is less automatized as compared to high-energy X-ray and proton therapy. This enhances the risk of errors [3]. It is therefore important to have strong treatment verification procedures. However, clinics do not perform sufficient treatment verification since relevant technologies are not available. Ongoing surveys from ESTRO indicate that OTV is performed in less than 10% of BT clinics although more than 80% would be interested, given a relevant system was available [4].
OTV for eBT is equally sparse for similar reasons, though equipment calibration uncertainties commonly exceed 10% [5]. A newly established EC-funded international consortium involving the major standard laboratories in Europe (PRISM-eBT) aims at improving this [6]. AUH is a member of PRISM-eBT and the PhD project will be linked to it.

In vivo dosimetry (IVD)

IVD is the most direct way to verify dose delivered during radiotherapy, as it measures the delivered dose in the patient. An IVD system has been developed by AUH together with MD Anderson Cancer Centre, US. The dosimeter consists of a scintillating crystal coupled to an optical fibre. It fits inside a

standard BT needle, thus enabling it to measure the dose inside patients. The high time-resolution of the system enables measurement of the delivered dose rate, providing OTV. The group has also developed algorithms to reconstruct the source position and 3D dose distribution based on these measurements [7,8]. This allows full comparison of the planned and actual dose delivered to volumes of interest. A clinical workflow has been developed in collaboration with the clinical staff at AUH, and an international multi-centre clinical study of real-time IVD for BT was initiated at AUH in 2015 as the first in the world. Currently the system works as stand-alone, which limits the usage. Lack of communication with the treatment planning and delivery system complicates comparison and treatment interruption in case of errors. Furthermore, the current positioning method causes too large an uncertainty. Integration of a similar system into the treatment delivery equipment (the so-called afterloader) would remove these limitations. The positional uncertainty can be reduced by introducing a detector positioning verification (DPV) system. A fully afterloader-integrated IVD and DPV system would simplify OTV thereby making it more accessible to for the BT community.

RESEARCH PLAN

Part 1: Afterloader-integrated Scintillation dosimeters (SD)

Aim

The aim of part 1 is to prove that SD probes can be produced small and robust enough to be handled by an afterloader, while maintaining high measurement accuracy.

Hypothesis

- The size of the current SD can be reduced by a factor of four while maintaining an accuracy of 3%.
- With the afterloader, the SD can be transferred in and out of a BT needle 100 times, losing no more than 5% of its signal strength.

Method

The SDs will be produced and characterised at AUH, who has produced several SDs based on fibre optic cables coupled to scintillating crystals. The cables usually have diameters of 0.5 mm or above. This must be reduced to 0.1 mm to gain the flexibility needed for afterloader integration. These dimensions are challenging since optical losses, light transition, and coupling stability all become larger concerns. Therefore thorough experimental analysis of the SDs' response to BT-sources will be performed in water phantoms. Several SDs must be made and investigated to determine their measurement reproducibility and accuracy. A SD feasible for IVD, will be integrated in an afterloader, and its real-time dosimetry capabilities characterised in a water phantom. The SDs' robustness will be stress tested, by sending them in and out of a needle 100 times using the afterloader.

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Feasibility

The research group holds a laboratory at Aarhus University (AU) equipped to produce the SDs. It will cooperate with the BT vendor, Elekta, to ensure optimal integration of the SDs in an afterloader. The BT treatment facilities at AUH are available to the research group and hold all relevant soft- and hardware for scintillator dosimetry. The applicant has produced and characterised several SDs during his master's project and thus has experience essential for this part of the project.

Impact

Dosimetry systems for BT are mainly stand-alone, requiring purchase of and educated personnel for separate treatment delivery and dosimetry equipment. An integrated IVD system simplifies purchase, daily use, and maintenance. Direct communication between delivery and verification systems will increase the quality of post-processed data, online comparison of delivered and planned dose, and equipment-initiated treatment interruptions. This will increase patient safety and availability of OTV with IVD.

Part 2: Dosimeter position verification (DPV)

Aim

The aim of part 2 is to develop a DPV system able to determine the position of a SD. It will consist of two optical fibres running along the SD from Part 1 in a shared cable.

Hypothesis

- The SD position inside a needle can be determined with 0.5 mm accuracy.
- A DPV system can be made with a diameter of <0.2mm, enabling it to be combined with the SD from part 1 in a single cable.

Method

A DPV system prototype will be made and characterised at AUH. Its accuracy will be investigated in a water phantom. Then the system will be scaled and combined with the SD produced in Part 1 in a single cable. If they are successfully merged an industrial partner will integrate them in an afterloader and the accuracy of the system will be investigated in a water phantom.

Feasibility

The research group's laboratory holds resources necessary for the production and investigation of the DPV system. Elekta has agreed to integrate the SD and DPV system of Part 1 and 2 in an afterloader.

Impact

A DPV system will greatly reduce the largest uncertainty component in current state-of-art dosimeters, improving the error detection capability of the system.

Part 3: IVD for eBT

Aim

Part 3 aims to prove the feasibility of using IVD for quality assurance during eBT.

Hypothesis

- A 3D dose map of the delivered dose from an eBT source can be determined with 5% accuracy.
- The dose rate for an eBT source can be measured in real-time with 5% accuracy.
- IVD can be performed for OTV during eBT without adding more than 30 min of additional workload.

Method

First the IVD system will be characterized for eBT to ensure 5% accuracy. Characterisation of detectors for eBT is a central part of the PRSIM-eBT project. This part of the project will be carried out in collaboration with the German metrology institute (PTB), the leading institution on PRISM-eBT. Short-term visits to PTB are planned for measurements at their laboratory, adding to measurements at AUH.
After a full characterisation, the SD will be used to measure dose distributions in a water phantom from different eBT sources. IVD during eBT will be tested by emulating a treatment in a phantom. Irradiation experiments will be performed both with and without simulated errors. The ability to verify a correctly delivered treatment and to identify errors will be evaluated. The IVD studies will be performed in collaboration with the clinical staff at AUH and used to develop a workflow for IVD during patient treatment. Once the workflow is tested in phantom studies, in vivo tests will be performed.

Feasibility

Characterisation of the SDs and time resolved measurements with eBT sources will be performed in the framework of the PRISM-eBT project, giving a solid foundation towards IVD during patient treatments. Department of Oncology, AUH, has agreed to provide resources needed including assistance from clinical staff.

Impact

It is important to bring IVD into eBT to gain data on the occurrence of errors in this modality and ensure that they are caught before the patient is harmed. Lack of official methods for calibration of new eBT equipment leads to large uncertainties in the dose delivery. PRISM-eBT aims to remove this uncertainty.

THE GROUP AND COLLABORATORS

The research group

All parts of the PhD project will be carried out by MSc Peter Georgi under supervision of associate prof. Jacob Johansen and prof. Kari Tanderup. The IVD research group at AUH was initiated in 2010 and currently involves a PhD (beside the applicant) and 3-5 undergraduate students. It is led by Jacob Johansen and includes students from physics, engineering and mathematics. It is one of the leading groups worldwide on BT IVD and the first to initiate clinical studies with real-time IVD for BT. The clinical study is performed in close collaboration with the clinical staff at AUH. The group holds a laboratory at Department of Physics and Astronomy, AU. The laboratory is fully equipped for production and testing of dosimeters. Furthermore, access to BT sources is available at AUH.

International and intersectorial collaborations

Part 1 and 2 of the project are performed in collaboration with the world's largest BT vendor, Elekta (Sweden). Elekta supports the project financially and will be actively involved in the integration of SDs into a test-afterloader. The applicant will have regular visits to the Elekta BT facility in the Netherlands. A longer stay of 1-2 months is planned as well. Furthermore, the group will collaborate with Danish companies with expertise in optics, regarding the coupling of the crystals.
Part 3 is linked to the PRSIM-eBT project and involves all the major standard metrology laboratories in Europe. The project is led by PTB, Germany. PTB has experience with both BT and eBT, and offers state-of-the-art equipment for high-precision measurements including dosimetry. Thorsten Schneider (PTB), who is coordinating PRSIM-eBT, has agreed to co-supervise the applicant on the eBT part of the project. Part 3 requires measurements at PTB, and the applicant will have 1-2 visits at PTB.
The clinical tests will be performed in close collaboration with the clinical staff at AUH (MDs and physicists).

IMPACT

BT is considered a safe treatment, but as with any other radiation modality, treatment errors do occur. The lack of OTV is therefore a clear hazard for patients. Focus over the last decade has been on developing dosimeters with high enough accuracy. This is now obtained, and next step is to prove that they can be integrated clinically with limited effort from clinics and clear improvement of patient safety. Having both IVD and DPV integrated in an afterloader provides an almost complete single system for delivering and monitoring dose, greatly simplifying BT sessions. More than 80% of BT

clinics have shown interest in OTV systems [4], and the proposed treatment system therefore has great commercial potential.

ETHICAL ASPECT

The majority of the project will be focused on phantom studies. The afterloader with an integrated IVD system will not be tested in patients during this project. If IVD will be performed for eBT, a written consent from the patients will be obtained.

TIME PLAN

The project time plan is shown on the last page.

REFERENCES

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[4] Spasic E and Kertzscher G, Preliminary results of GEC ESTRO surveys on treatment verification and IVD in BT in 55 European clinics.
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[6] Primary standards and traceable measurement methods for X-ray emitting electronic brachytherapy devices. https://www.euramet.org/research-innovation/search-research-projects/details/project/primary-standards-and-traceable-measurement-methods-for-x-ray-emitting-electronic-brachytherapy-devi/.
[7] Johansen JG et al., Time-resolved in vivo dosimetry for source tracking in brachytherapy. Brachytherapy, 2018;17:122-132.
[8] Jørgensen EB, Dosimetric impact of needle movements in HDR-BT treatments of the prostate. Master thesis 2018 (Available at the Library, Institute of Physics and Astronomy, Aarhus University).

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