Contribution ID: 77 Type: Oral

Preparations for the first veterinary trials of synchrotron radiation therapy

Thursday, 22 November 2018 15:45 (30 minutes)

The aim of our research is to undertake the first large animal trial of Microbeam Radiation Therapy (MRT) at the Australian Synchrotron to treat spontaneous cancers. The Imaging and Medical Beamline (IMBL) at the Australian Synchrotron is one of only four facilities in the world expressly designed to enable the clinical application of synchrotron radiotherapy for cancer patients. There are new robotic positioning systems recently installed at the IMBL now which are capable of positioning large animals and humans in the synchrotron beam for radiotherapy purposes. We will use this new capability and our existing medical physics research program to treat canine tumours with synchrotron radiotherapy. This has never been attempted before and we anticipate this proof-of-concept work will directly lead to clinical trials in humans for certain unresponsive, or recurring cancers where conventional radiotherapy has failed.

Synchrotron MRT is an experimental form of radiotherapy that is fundamentally different to conventional radiotherapy (CRT) [1, 2]. There is emerging evidence that synchrotron MRT is more effective in destroying tumours than CRT and has fewer side effects than CRT [3-6]. There is therefore potential for MRT to significantly improve outcomes for cancer patients. The long-term aim of our project is to translate MRT to a clinical reality. At present, MRT can only be performed using a synchrotron, which is not achievable at hospitals. As a pre cursor to clinical trials, we propose veterinary trials of synchrotron radiation with real, spontaneous cancers in dogs in close collaboration with our veterinary colleagues.

Our aim in 2019 is to plan and treat approximately 9 live dogs with spontaneous tumours. Our preferred, initial target will be skin tumours or bone tumours in the legs of the dog. These tumours are easy to locate and position in the synchrotron beam. For this pilot study, we will select small tumours that are located at shallow depths in order to maximise the dose coverage. We will do a simple dose escalation ('3+3 study') whereby we irradiate 3 dogs with a low dose (e.g. an integrated dose of 8 Gray in a single fraction) followed by an approximately 20% increase in the dose to 10 Gy for the next 3 dogs. We will increase to 12 Gy for the next 3 dogs if the acute radiation toxicity is minimal.

We will consider the project a success if we can safely and verifiably deliver a low dose (palliative dose) of synchrotron radiation to live (sedated) dogs using the robotic couch at the IMBL. If this pilot study is successful we will have made major steps towards initiating a new radiotherapy paradigm with synchrotron radiation; the significance of such an outcome for cancer patients everywhere cannot be overstated. There are some brain and lung cancer patients for example who have failed current treatments and have few if any treatment options available to them. Synchrotron MRT may offer hope to these patients. Our group has over 10 years'experience of Synchrotron MRT experiments using mouse models of healthy and malignant tissue. We now want to progress from our mouse model work (with artificial tumours) to larger animals with real, spontaneous tumours (e.g. pet dogs). Such work will be an invaluable proof of concept before we attempt MRT in human cancer patients.

In recent years, we have made tremendous progress towards realising our goals, most notably in the medical physics area. We have commissioned a computerised Treatment Planning System [7], completed a protocol for measuring the absorbed dose from the synchrotron radiation [8, 9], and developed sophisticated image-guided radiotherapy protocols [10]. Our work is at the stage now where we can plan and treat a dog on the robotic positioning system on the IMBL. In the

radiobiology field, we have systematically characterised the toxicity of MRT for a range of treatment sites which is crucial for choosing safe doses for our proposed veterinary trials [11]. In recent work (April & July 2018) we planned and irradiated a dead lamb and dog with conventional (uniform) and microbeam radiation fields to test the physical components of the beamline.

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Session Classification: Parallel Session 8

Track Classification: Radiotherapy