RADIOBEAM

A microfluidic in-vitro perfusion-cell for radio-oncological pharmaceutical testing

Luc Stoppini

Brief description

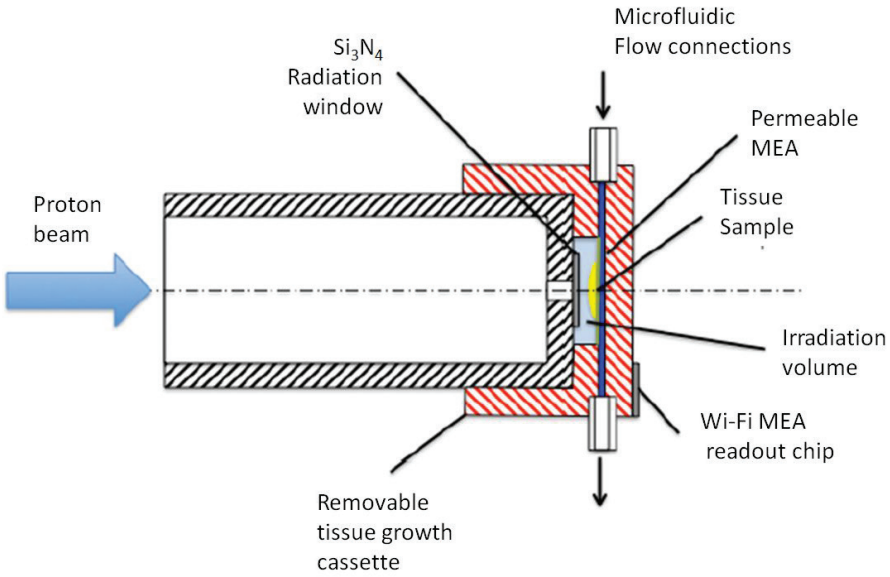
In collaboration with Prof Harry James Whitlow from the Ionlab-Arc and the clinician Dr. Pierre-Yves Dietrich from the Geneva University Hospitals (HUG), we have developed an in-vitro microfluidic perfusion cell for radiopharmacological testing with human neural tissue cultures that allows proton-irradiation under conditions representative of the site of tumour eradication deep inside the patient's body. This new in vitro model will be an important tool for the development of drug used in cancer therapy.

Key points

The main novelties is to use "small" MeV accelerator for 3 MeV protons instead of large 250 MeV clinical accelerator facility in order to irradiate human tissue samples in a microfluidic cell needed to speed-up the drug development in the oncotherapy field.

Main innovations:

- to perform drug development without the need for Ion Beam Cancer Therapy facility.
- in-situ real-time studies now possible.
- capability to directly study pharmaceutical effects.
- no need to use human or animal models.
- low-cost technologies.



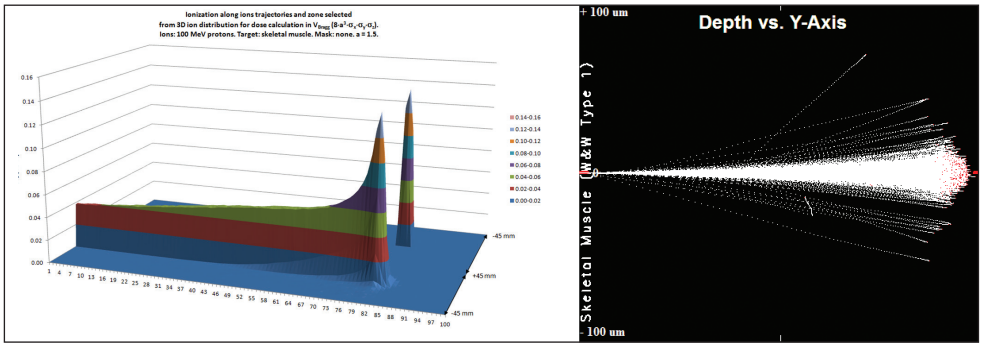
Ion Beam proton accelerator.

In vitro model of brain tumours: Luc Stoppini has demonstrated that neural progenitors derived from induced pluripotent stem cells grown at air-liquid interface on porous membrane can generate 3D brain tissue-like structure. He also showed that those 3D neural tissues were functional by recording electrophysiological activities. A new in vitro approach to reproduce features of the brain tumour disease, in particular by using glioblastoma cells which is an aggressive brain tumour characterized by its high propensity for local invasion, formation of secondary foci within the brain, as well as areas of necrosis.

This engineered 3D in vitro approach, will provide a relevant model to study the disease and will allow us to study the effect of proton and carbon ions irradiations to specifically induce a selective destruction of cancer cells in combination with radiosensitisers and sparing the normal brain tissue surrounding the tumour.

Ion irradiation research and technology The Ionlab-Arc group focuses on work around the 1.7 MV Tandetron accelerator. The proton generated by the ionbeam will damage the DNA which in turn leads to eradication of tumours. Ionlab-Arc have developed a technical know-how on ultra-thin Si3N4 windows partly supplemented by high-resolution gas ionisation detectors.

The tissue growth cassette has been designed and prototypes have been tested. We are now in the phase of the irradiation of healthy neuronal cells. The glioblastoma cells and the healthy neuronal cells have been co-cultured with success. Irradiation of this brain glioblastoma tumour in vitro model will be tested with radioprotector and radiosensitiser.



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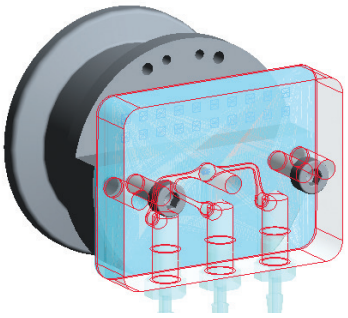

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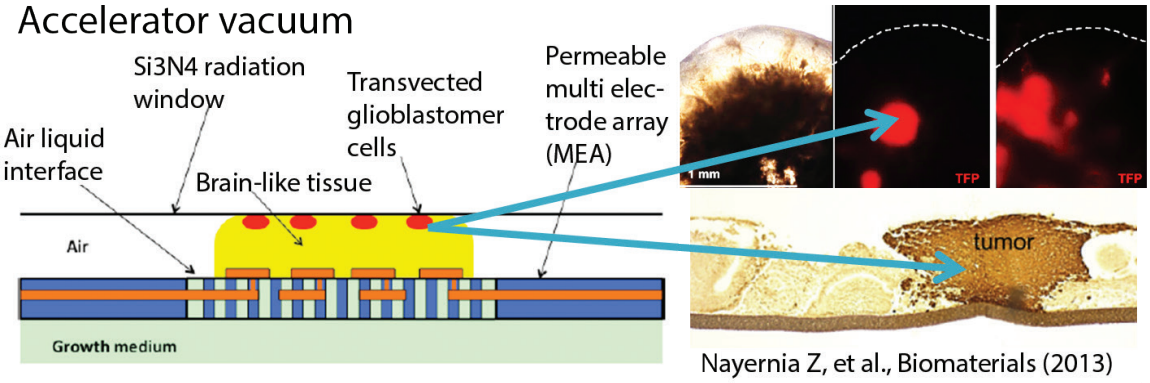

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Output

Tools and method developed will drastically reduce the need for animal model testing in radiopharmaceutical drug development.

Provide tools for developing tests for “after the disaster” biological dosimetry.

In collaboration with clinicians like Dr. Pierre-Yves Dietrich from the Geneva University Hospitals (HUG), we will evaluate the potential cost-reduction for Ion Beam Cancer Therapy treatment by allowing lower doses and fewer fractions.

Publications:

Norarat R., Guibert E., Jeanneret P., Dellea M., Jenni J., Roux A., Stoppini L., Whitlow H. J. A gas ionisation direct-STIM detector for MeV ion microscopy. Nuclear Instruments and Methods in Physics Research B 348 (2015) 58–61

Special equipment

The RadioBeam project use 1.7 MV Tandetron accelerator for the formation of ion beam. This accelerator from the HE-Arc is run by the Ionlab-Arc group, directed by H. J. Whitlow.

Legend

1 - Protons distribution into human skeletal muscle to select the Bragg peak in the 2D ionization matrix.
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2 - Adaptor and tissue growth cassette with microfluidic.
3 - Left panel: Schematic view of the cassette Right panel: brain tumor model.
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h e p i a
Haute école du paysage, d’ingénierie et d’architecture de Genève
Ra&D
Rue de la Prairie 4
CH - 1202 Genève
Tél. +41 (0)22 546 24 00
rad.hepia@hesge.ch
www.hesge.ch/hepia