UNIVERSITY OF BIRMINGHAM

NPL National Physical Laboratory

Development of instrumentation for dosimetry of spatially and temporally fractionated beams

Centre for the Clinical Application of Particles
24/06/2020

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Contents

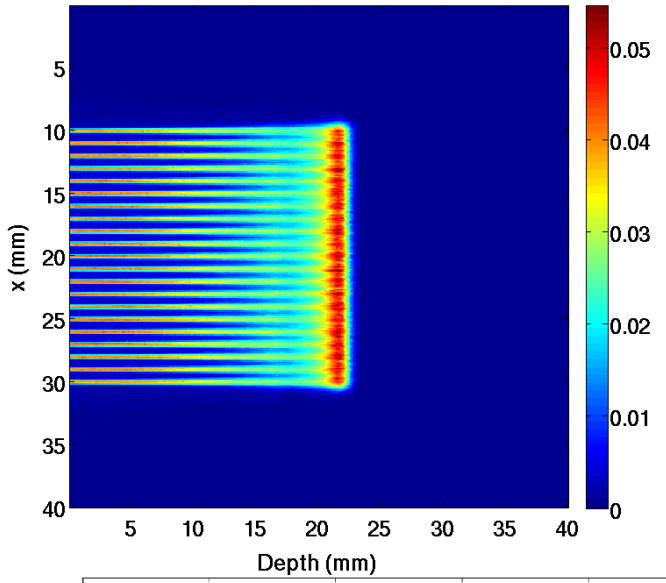
- Introduction to spatial fractionation
  - Why this is of interest
  - Focus of microbeam (as most challenging)

- Current results with a CMOS sensor
  - Comparison to existing technology

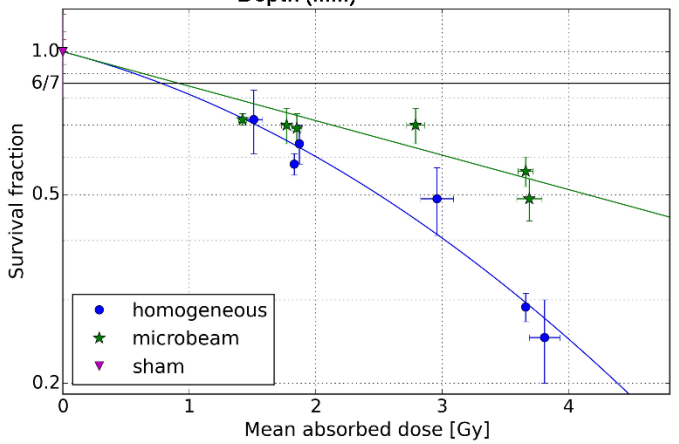
- Future outlook
  - Adaption to protons
  - Further ambitions

Microbeam radiotherapy: Introduction

- Narrow beams of radiation (< 500 μm) spatially fractionated within patient delivered in a grid pattern (also relevant to minibeam)
  - Non-cancerous tissue can withstand higher dose levels enabling treatment of radiation resistant tumours that are hard/impossible to treat otherwise
  - Preclinical studies have shown greater efficacy compared to conventional broad-beam radiotherapy, with little to no side effects
- Due to multiple Coulomb scattering, proton microbeam/minibeam radiotherapy has added effect of uniform dose delivery in the tumour volume



Simulated proton microbeam collimator: http://faculty.washington.edu/juergen/proj_pMRT.html



Dose-dependent survival fraction of CHO-K1 cells to 25 kVp X-Ray Beam, doi: https://doi.org/10.1371/journal.pone.0186005.g003

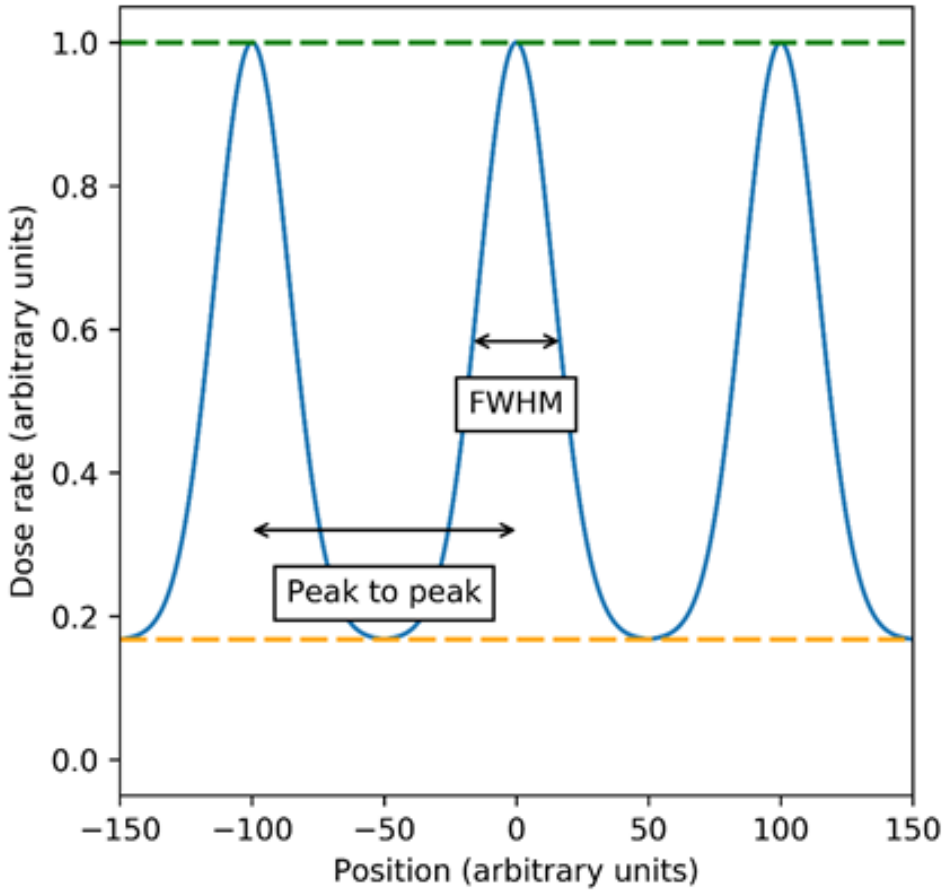
Microbeam radiotherapy: Challenges

Parameters shown to influence treatment outcome:

Peak to peak separation	50 – 200 um
Beam FWHM	25 – 100 um
“Peak-Valley-Dose-Ratio”	10 - 400
Dose rate delivered	0.001 – 100 Gy/s
Total dose	60 – 600 Gy
Radiation modality	X-rays/ Protons

Very influenced by specific tumour biology with possible explanations:

- being preferential damage to tumour vasculature
- radiation-induced bystander and abscopal effects



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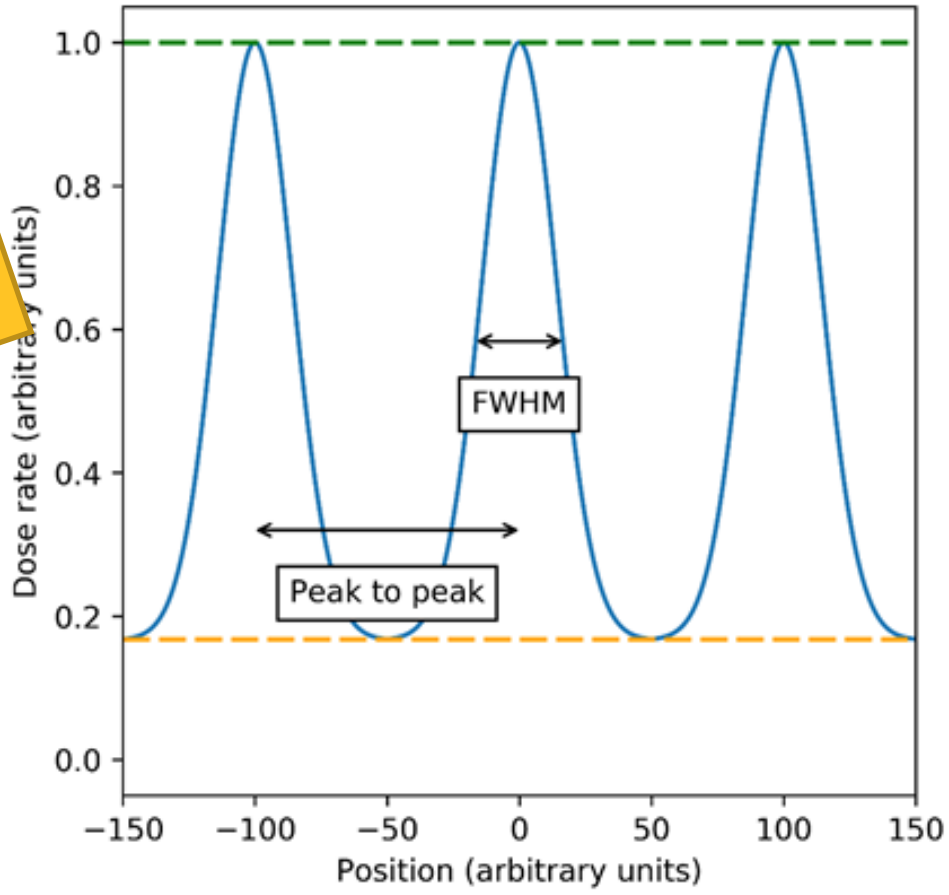

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Choice of instrumentation: vM1212 CMOS detector

- Large format pixelated CMOS sensor
- Designed for medical and scientific x-ray imaging by the CMOS Sensor Design Group at the Rutherford Appleton Laboratory
- Manufactured by vivaMOS Ltd. UK.

Pixel pitch	50x50 um^2
Active area	6 x 6 cm^2
Water equivalent thickness	~ 0.5 mm
Frames per second	34
Predicted radiation tolerance	>10kGy

- Using it for PhD project to provide independent beam monitoring for the NPL Proton Calorimeter

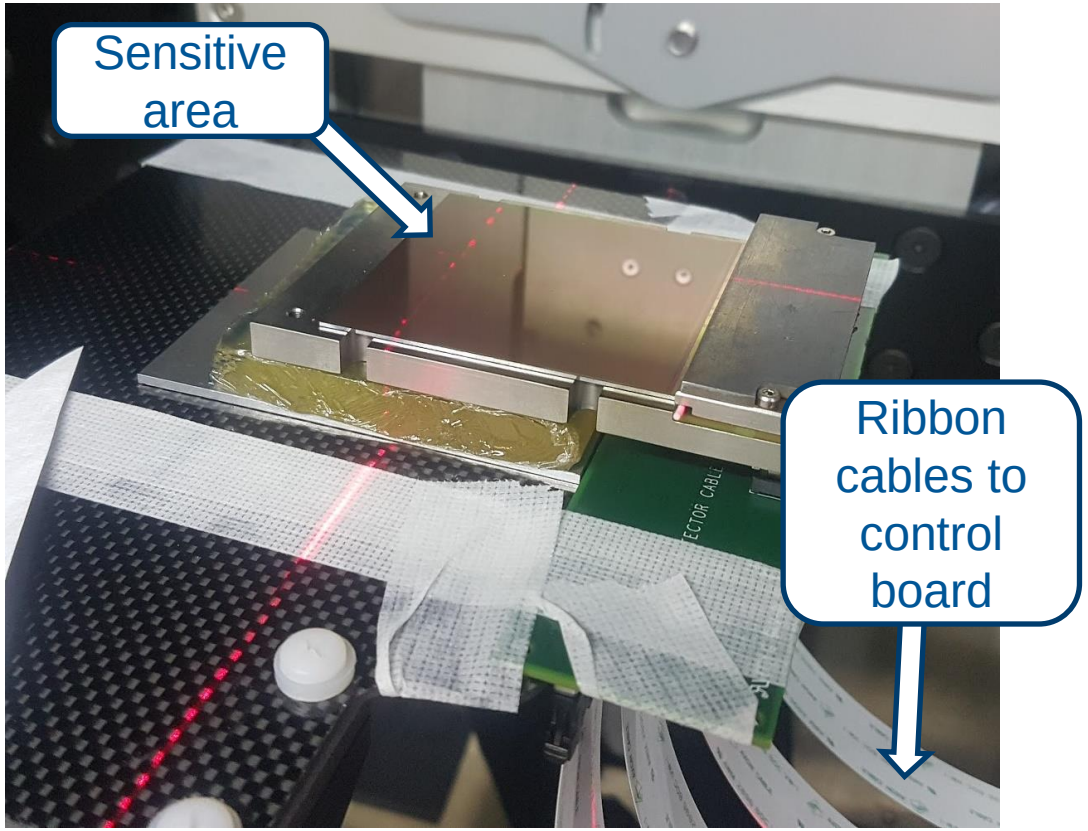
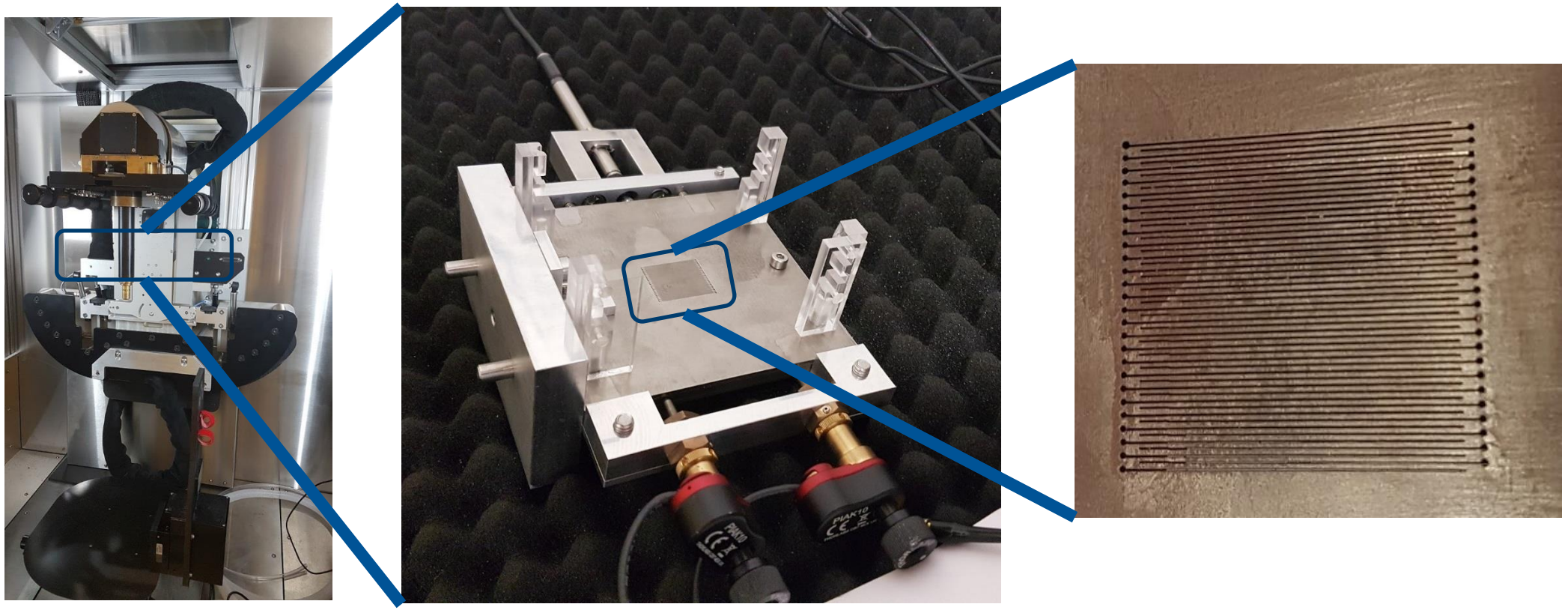


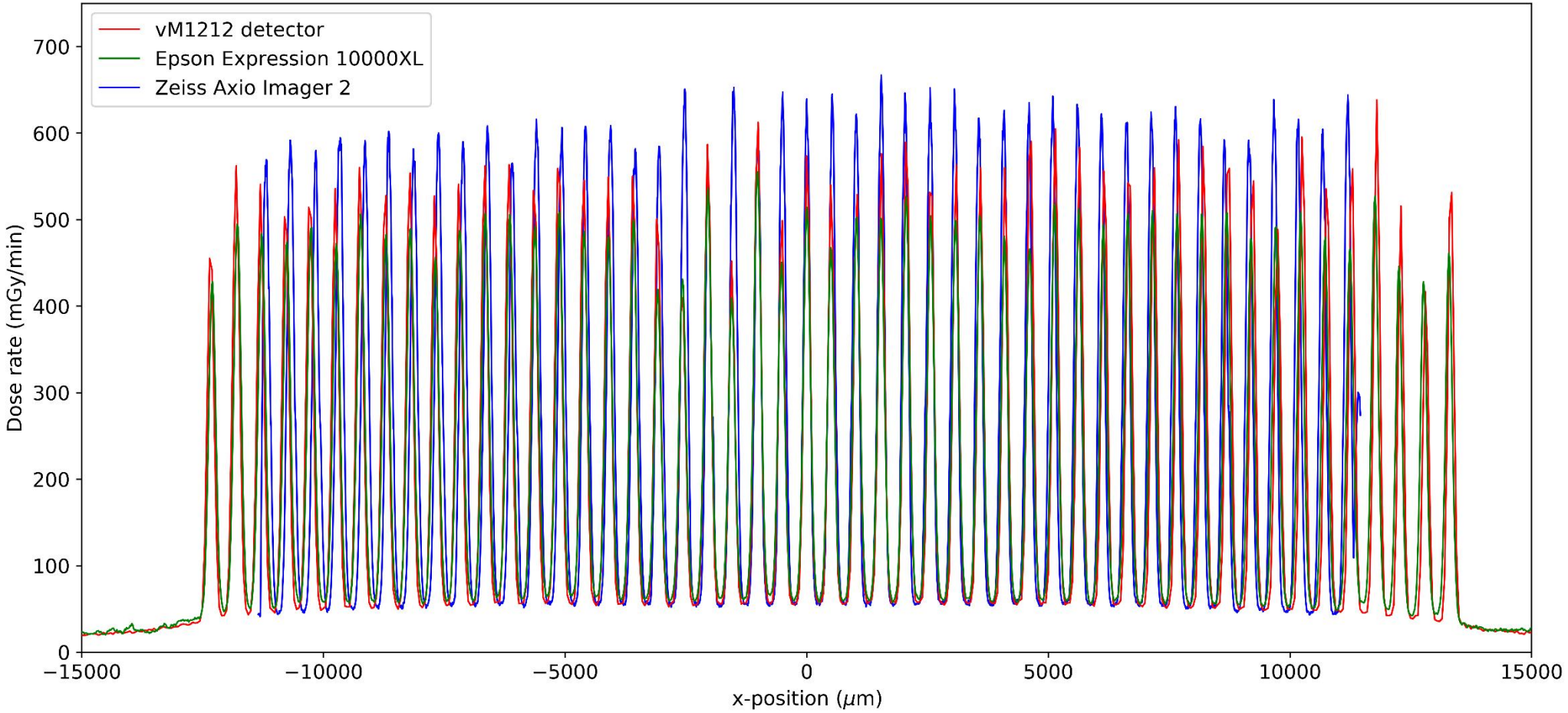
Image of vM1212 detector

X-ray microbeam radiotherapy investigation: Facilities at Technical University of Munich



Stefan Bartzsch *et al.* at the Technical University of Munich developed an adjustable microbeam collimator for a Small Animal Radiation Research Platform (SARRP) for preclinical investigations, capable of changing the nominal slit width between 0 – 100 µm

Microbeam radiotherapy investigation:
CMOS (real time) vs Film (Scanner + Microscope)



Microbeam radiotherapy investigation:
CMOS (real time) vs Film (Scanner + Microscope)

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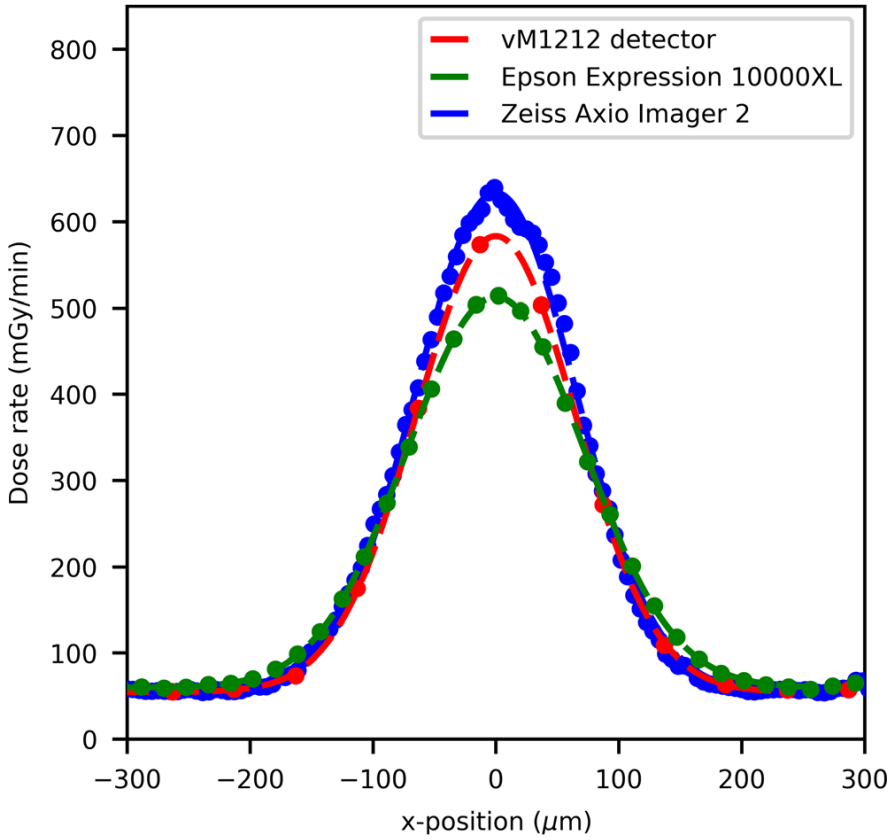
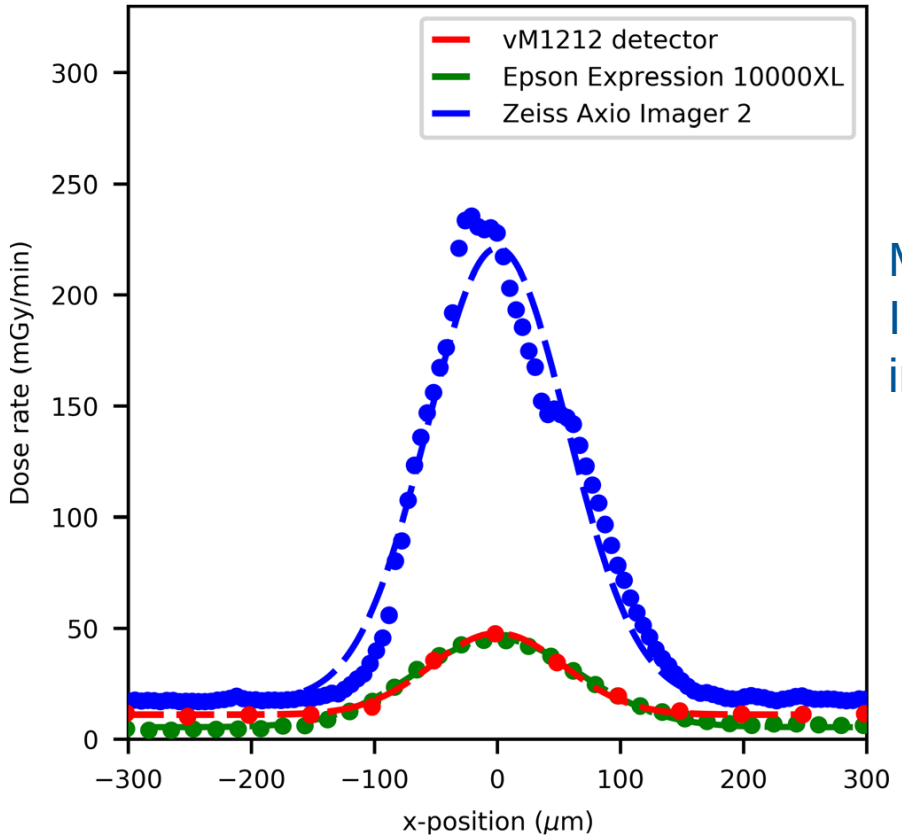
100 um nominal slit width



25 um nominal slit width



Microscope (Zeiss Axio Imager 2) was obtained in a different run

Microbeam radiotherapy investigation: Dynamic (real time) results

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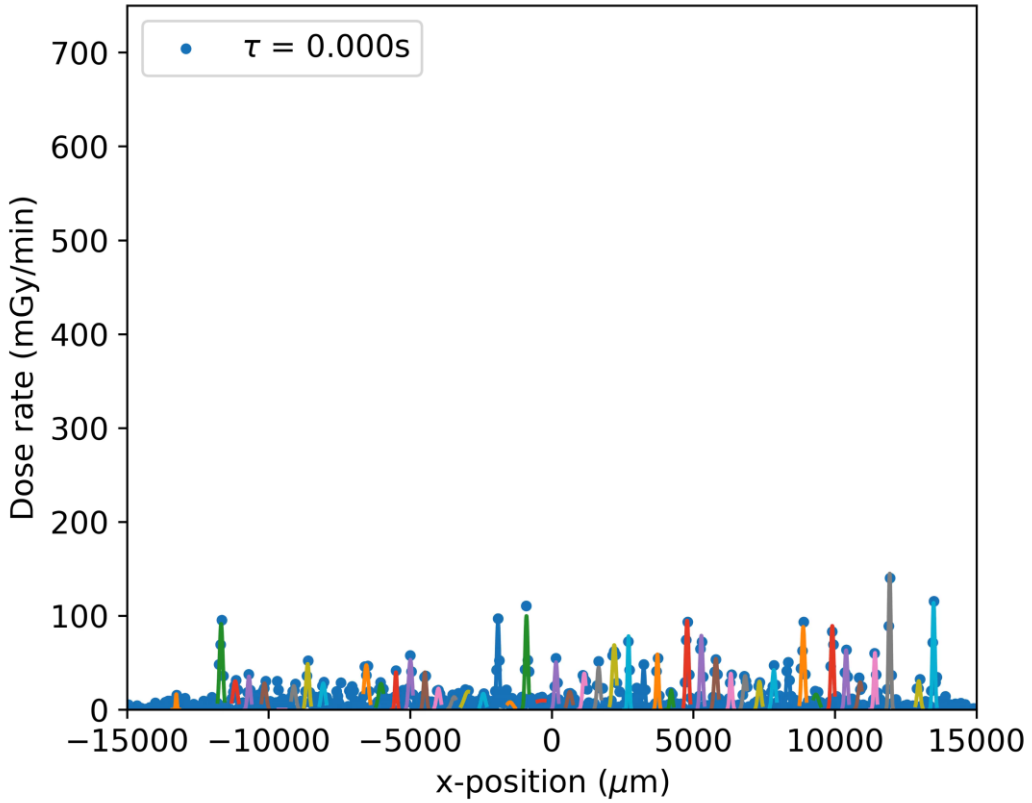
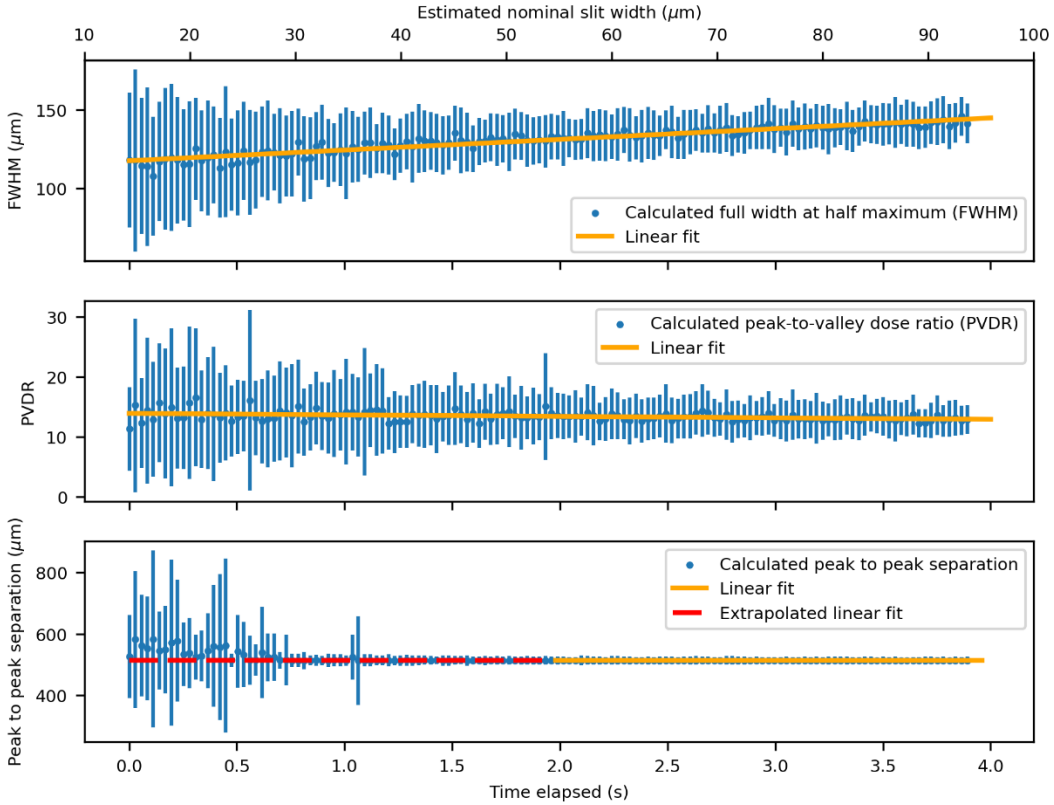
Opening microbeam slit



Calculated microbeam parameters



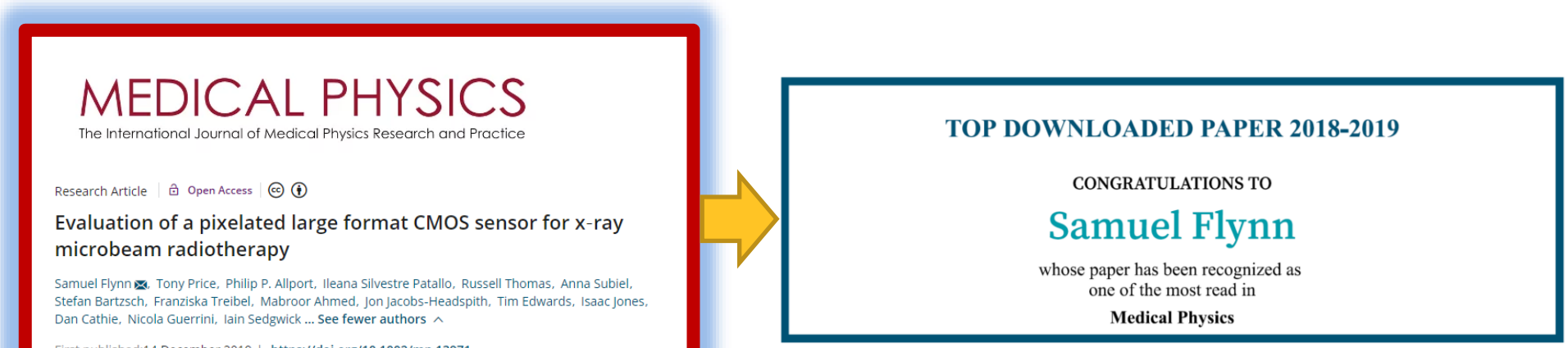
Backup: https://youtu.be/F33O2cMaVv4

Future outlook

- Reproduce in proton beams
  - Use new microbeam/FLASH facility at Birmingham
- Explore smaller pixel sizes
- Look at larger sensors (12 cm x 14 cm LASSENA)
- Study dynamic range limitations
- Faster readout
  - ~10 ms resolution currently achievable, would like to push further for FLASH
- Radiation tolerance
  - Good to few 100 kGy but need testing beyond that
  - Need to develop more radiation-hard designs to withstand up to $10^{15} n_{eq}/cm^2$ bulk damage*

*Working with CERN and STFC on more tolerant process, see: “Mini-MALTA: radiation hard pixel designs for small-electrode monolithic CMOS sensors for the High Luminosity LHC” Dyndal *et. al.* 10.1088/1748-0221/15/02/P02005

More information



First demonstration of real-time in-situ dosimetry of X-ray microbeams using a large format CMOS sensor Nuclear Instruments and Methods in Physics A, 2020 *(in press)*

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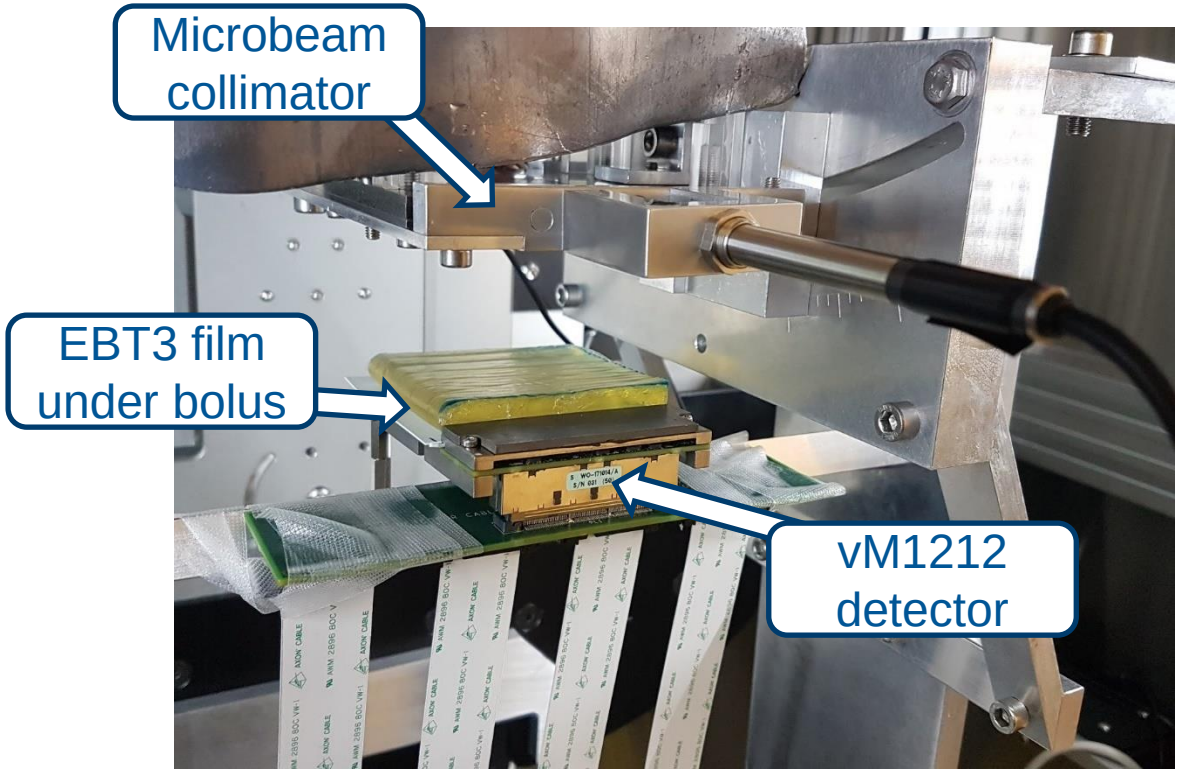
This work was supported by the Science and Technology Facilities Council (grant ST/ P002552/1) and by the UK government's Department for Business, Energy and Industrial Strategy.

Spare slides

Microbeam radiotherapy investigation: Methodology



1. Determined reference conditions within the SARRP
2. Calibrated response EBT3 film and vM1212 detector to calibrated ionisation chambers (with appropriate build-up and backscatter)
3. Delivered static fields at known nominal slit widths to film and detector at the same time

Compared detector response to EBT3 film using optical microscopy (4 um resolution)

Additionally: Delivered moving fields to detector only