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# X-Tream: a novel dosimetry system for Synchrotron Microbeam Radiation Therapy

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# X-Tream: a novel dosimetry system for Synchrotron Microbeam Radiation Therapy

# Abstract

Microbeam Radiation Therapy (MRT) is a radiation treatment technique under development for inoperable brain tumors. MRT is based on the use of a synchrotron generated X-ray beam with an extremely high dose rate (~ 20 kGy/sec), striated into an array of X-ray micro-blades. In order to advance to clinical trials, a real-time dosimeter with excellent spatial resolution must be developed for absolute dosimetry. The design of a real-time dosimeter for such a radiation scenario represents a significant challenge due to the high photon flux and vertically striated radiation field, leading to very steep lateral dose gradients. This article analyses the striated radiation field in the context of the requirements for temporal dosimetric measurements and presents the architecture of a new dosimetry system based on the use of silicon detectors and fast data acquisition electronic interface. The combined system demonstrates micrometer spatial resolution and microsecond real time readout with accurate sensitivity and linearity over five orders of magnitude of input signal. The system will therefore be suitable patient treatment plan verification and may also be expanded for in-vivo beam monitoring for patient safety during the treatment.

#### **Keywords**

synchrotron, x, microbeam, tream, radiation, therapy, novel, dosimetry, system

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ABSTRACT: Microbeam Radiation Therapy (MRT) is a radiation treatment technique under development for inoperable brain tumors. MRT is based on the use of a synchrotron generated X-ray beam with an extremely high dose rate (~20 kGy/sec), striated into an array of x-ray micro-blades. In order to advance to clinical trials, a real-time dosimeter with excellent spatial resolution must be developed for absolute dosimetry. The design of a real-time dosimeter for such a radiation scenario represents a significant challenge due to the high photon flux and vertically striated radiation field, leading to very steep lateral dose gradients. This article analyses the striated radiation field in the context of the requirements for temporal dosimetric measurements and presents the architecture of a new dosimetry system based on the use of silicon detectors and fast data acquisition electronic interface. The combined system demonstrates micrometer spatial resolution and microsecond real time readout with accurate sensitivity and linearity over five orders of magnitude of input signal. The system will therefore be suitable patient treatment plan verification and may also be expanded for in-vivo beam monitoring for patient safety during the treatment.

KEYWORDS: Radiotherapy; Dosimetry concepts and apparatus; Detector control systems; Synchrotron X-rays.

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#### Contents

1. Introduction	1
2. X-Tream dosimetry unit: system architecture	3
2.1 MRT Dosimeter	4
2.2 Preamplifier module	4
2.3 Central data acquisition System Unit	5
2.4 MRT Graphical User Interface - RadPlot	7
3. Experimental results and discussion	7
3.1.1 System response characterization: Slew rate	8
3.1.2 Conversion factor and electronics response linearity	9
3.1.3 Noise performance	10
3.2 Application of X-Tream in MRT: microbeam array measurement	11
4. Conclusion	13

# **1. Introduction**

The development of synchrotron light sources with X-ray intensities several orders of magnitude higher than conventional X-ray tubes, has allowed the introduction of a unique experimental technique for the radiation treatment of inoperable and otherwise untreatable brain tumours [1]-[2]. Since 1992, this new radiation oncology treatment modality has been under development at the Brookhaven National Laboratory (BNL) [3] and soon after at the European Synchrotron Radiation Facility (ESRF) [4]. Such radiation treatment, commonly referred to as Microbeam Radiation Therapy (MRT), uses a synchrotron generated X-ray beam physically collimated into an array of microbeams, each (microbeam peak) being few tens of microns wide with a pitch of a few hundred microns. The very high intensity allows MRT to use X-rays with energies (50-350 keV) that are more typical of diagnostic X-ray techniques rather than the megavoltage X-ray energy beams produced by hospital linear accelerators, commonly used in radiotherapy. The treatment dose can be delivered in a single, unidirectional fraction or in several fractions via crossfiring or interlacing [5]. Crossfiring of the X-ray microbeams, e.g. two orthogonal directions, leads to a considerable radiation dose in the targeted cancer volume as it is positioned at the microbeam array intersection point. The total target dose is therefore delivered in two dose fractions, with a delivery time of up to a few seconds each. MRT beam dosimetry is currently carried out using combination of Gafchromic film and ionisation chambers [6]. These techniques, however, have limitations: films are not real-time, have a limited dynamic range (so cannot resolve the MRT valley and peak doses simultaneously) and need several hours for the polymerization process to stabilize. Ionising chambers provide realtime dose measurements but do not have the necessary spatial resolution for profiling such narrow X-ray beams and therefore cannot be used in the real treatment configuration of MRT. A full account of other dosimetric techniques used in MRT is given in Brauer-Krisch [7].

The Centre for Medical Radiation Physics (CMRP) has been involved in the dosimetry of MRT since 1996. The preliminary technique included the use of MOSFET sensors, which display exquisite spatial resolution (typically 0.1 microns), are able to resolve accurately the dose distribution of the microbeams and have real-time readout capability [8]-[13]. The limitation of this approach was due to the extremely high dose rate in the proximity of the microbeams. The practical use of the MOSFET in a clinical scenario is limited by the saturation of its dose response. MOSFET annealing techniques at CMRP are currently under development.

The optimal specifications for the dosimetry system required for a clinical radiation scenario in MRT are that the system should display a wide dynamic range of approximately  $10^5$  (so as to be able to measure accurately, the instantaneous dose rate (up to 20 kGy/s) in the microbeams and the valley between microbeams [14], a micron-sized spatial resolution (to be able to resolve the microbeam width of 50 to 100µm and the microbeam pitch of approximately 400µm), and the ability to evaluate the main parameters of the beam in real-time to check the quality of the beam and accuracy of the mechanics for pre-treatment Quality Assurance (QA). Recently CMRP has introduced a new approach to cope with these dosimetry specifications known as X-Tream, an X-ray treatment monitoring system, the architecture of which is illustrated in Fig. 1. The architecture discussed in this paper is a simplified version of the final design which will include the use of a system to move the detector relatively to the phantom to match closely the real clinical scattering conditions.

X-Tream is a quality assurance system which consists of two distinct modules:

- On-line microbeam Monitoring Unit (OMU): this sensor is a multichannel detector with high spatial resolution which monitors the instantaneous X-ray flux in each microbeam and each valley between microbeams, simultaneously during treatment. A safety trigger pulse is generated if a degradation of the microbeam intensity profile is sensed (as illustrated in Fig. 1a). This system is designed to make the radiation treatment safer by limiting the X-ray exposure time of the patient to a few milliseconds (primarily limited by the time required to dump the electron beam in the storage ring).
- 2. X-Tream dosimetry unit: this sensor and readout system is developed specifically for MRT dosimetry typically in water or solid water phantoms. The sensor is based on a single thin microstrip silicon detector which can be moved at a constant speed laterally across the radiation field. During the scan, the dose rate detected by the sensor is sampled, recorded and analysed by a fast data acquisition system. It is therefore able to measure the lateral dose distribution of the microbeams and the valleys at a particular depth in a phantom. It also calculates, on-line, all the relevant parameters for quality assurance of MRT such as the Peak-to-Valley Dose Ratio (PVDR), peaks/valleys position identification and alignment and peak shape in the few seconds it takes to scan across the radiation field.

In this work the principle of operation of the X-Tream dosimetry unit is described and discussed along with the characterisation of the system's performance on the biomedical beam line ID17 at the ESRF. The performance of the OMU will be discussed as the focus of a separate article.

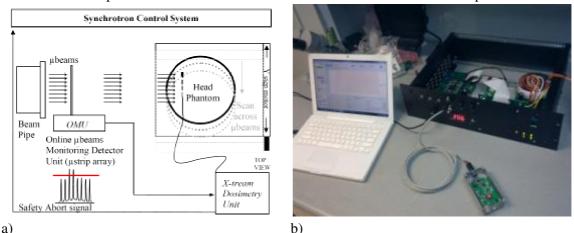


Fig. 1: a) Architecture of X-Tream; b) picture of the X-Tream dosimetry unit with the preamplifier and the software running on a laptop.

# 2. X-Tream dosimetry unit: system architecture

The prototype is composed of three main parts: the silicon sensor probe, the preamplifier and the Central data acquisition System Unit (CSU) as shown in Fig.2. The CSU provides high voltage bias, the digital conversion of the measured detector response signal (radiation induced photocurrent) and the communication interface with the remote personal computer by a standard USB2.0 link. The system is fully remotely controlled by RadPlot, a custom designed graphical user interface developed in C++ discussed in more detail below.

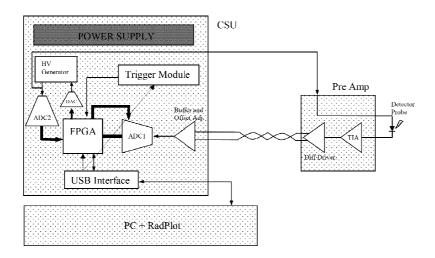


Fig.2: X-Tream dosimetry unit; the detector probe has been represented by a diode readout by the preamplifier module and biased by the High Voltage generator.

#### 2.1 MRT Dosimeter

A main challenge to be addressed in MRT real time dosimetry relates to the highly striated radiation field which includes, typically, up to 70 X-ray microbeams (each being 50  $\mu$ m wide) with a pitch of 400  $\mu$ m. The spatial resolution of the dosimeter therefore needs to be of the order of 10  $\mu$ m in order to satisfy the dosimetry requirements of MRT.

The core of X-Tream dosimetry unit is the sensor as shown in Fig.3. The detector is composed of a single microstrip (10 $\mu$ m wide) silicon diode fabricated on a 100  $\Omega$ -cm p-type 50  $\mu$ m thick epitaxial substrate. The chip is 1.5x1.0 mm<sup>2</sup> and the epitaxial layer is grown on top of 370  $\mu$ m thick p-type 0.001  $\Omega$ -cm silicon substrate. It can be used in passive mode or polarised up to 200 V; its structure incorporates also an n+ guard ring which limits the sensitive area to approximately 30  $\mu$ m at 50 V. The proposed geometry is represented schematically in Fig.3b.

In this development, special attention has been paid to find a solution to minimise the dose enhancement due to the surrounding materials of the silicon detector (shown in Fig. 3): the packaging design, patented by CMRP, so named "Drop-in" technology, consists of a kapton probe 600  $\mu$ m thick, 10 mm wide and 300 mm long which embeds the silicon sensor (shown in Fig.3c). The sensor chip has been connected to the probe by a flexible carrier which consists of a thin polyamide supporting substrate with a thin, chemically deposited, aluminium layer and tab bonded to the detector's pads and to the probe's tracks (shown in more detail in Fig.3a). The design allows the use of the probe within a water tank or tightly embedded in solid water phantoms and makes the detector very adaptable to several different QA procedures.

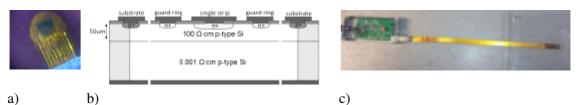


Fig.3: a) Single microstrip silicon detector embedded in the kapton probe using the Drop-in technology; b) Diagram of the cross section of the sensor; c) picture of the kapton probe and the preamplification module.

#### 2.2 Preamplifier module

An MRT dosimetry readout system must be able to estimate the dose rate in the peaks and in the valleys between the microbeam peaks. The main parameters which have driven the design of the preamplifier have been the signal dynamic range and the equivalent capacitance at the frontend input. The PVDR predicted by Monte Carlo radiation transport simulations of a typical microbeam array consisting of 51 microbeams at the surface of a solid water phantom is few thousand [15] and represents a very challenging scenario in terms of dynamic range required of the preamplifier. A minimum dynamic range for the dosimeter is therefore 10<sup>4</sup>.

Adding to this complication is the capacitance of the detector embedded in the kapton probe and its effect on the dynamic range. A capacitance of 7pF has been measured at 50V for the silicon detector shown in Fig. 3. Despite the significant capacitive node at the input, the desired preamplifier should maintain a dynamic range of greater than  $10^4$ . In addition, the preamplifier must maintain sensitivity linearity over the full dynamic range and also display wide bandwidth to correctly measure the input signal variation from the detector. The use of a logarithmic amplifier, despite the wide dynamic range, is possible, but not highly recommended because of the strong dependence of the preamplifier characteristic to the temperature which affects strongly the linearity of the response.

The photocurrent generated in the sensitive volume of the sensor by the X-ray beam is, in principle, directly proportional to the MRT dose rate. The desired input signal dynamic range is then of the same order of magnitude as the expected dose rate. The frontend preamplifier architecture which best suits the above requirement is a transimpedance amplifier with a gain of approximately 10<sup>5</sup>. Moreover the input stage impedance must match the equivalent probe capacitance and must minimize the input leakage current so as to reduce the output offset of the preamplifier. The solution proposed is based on a commercial JFET input stage operational amplifier with cascode compensated architecture (AD795) from National Semiconductor. The preamplifier module was designed so that it could be connected to the CSU by a long cable to allow the positioning of the preamplifier close to the probe and the phantom. Noise rejection and analog signal integrity was achieved by the use of a differential amplifier pair driver/receiver (EL5172/EL5072) from Intersil.

# 2.3 Central data acquisition System Unit

Typically there is significant distance between the experimental hutch and the control room in synchrotron MRT, and as such, remote control of dosimetry instrumentation is essential. The central system unit (CSU) controls the acquisition of the differential signal generated by the preamplifier, the offset adjustment, the digital conversion of the signal, the high voltage bias of the detector and the regulated bias for all the electronic components.

The core of the CSU is the Field Programmable Gate Array (FPGA) Spartan-3 (XC3S400-4PQ208C) manufactured by Xilinx and equipped with a Cypress chip (CY68013) for implementation of the USB2.0 interface. The system also has a Cypress PLL (CY22150), which provides the clock synchronisation of the I/O buses and the generation of the internal clocks. The firmware has been designed in the descriptive language Verilog [16], [17].

Fig.4 is a schematic representation of the firmware architecture implemented into the FPGA: the digital clock manager (DCM), fed by the main clock from the PLL at 140MHz, generates all the time bases of the CSU. The DCM's main task is the synchronisation of the FIFO blocks which have the input at 20 MHz and the output bit stream at 48 MHz. Each word stored in the FIFO is composed by a 16 bit header followed by 16 bit ADC-data; the ADC-data (sampling rate is 1 MHz) are represented by integer numbers proportional to the amplitude of the current.

The *START* signal from the USB interface produces the activation of the state machine which controls the ADC for the acquisition of the current signal from the detector. It also enables the acquisition chain and the FIFOs through the DCM.

Two asynchronous modules control the high voltage bias of the detector by a DAC to set the value of the switching regulator and by an ADC to check if the applied value is correct; once the value has been confirmed by the operator, the bias can be applied safely to the detector pin. All the controls and indicators are implemented into the graphical interface developed at CMRP known as RadPlot.

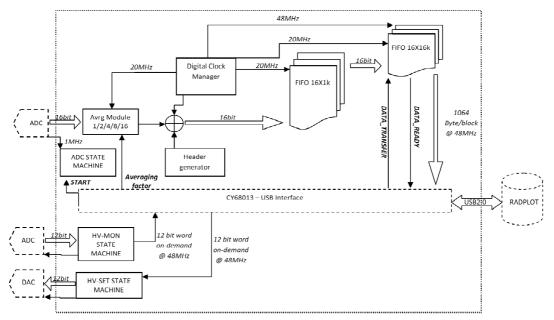


Fig.4: Schematic diagram of the firmware and main functionalities of the FPGA module; the blocks with dashed contours represent external components.

The AvrgModule, controlled directly by the software interface, calculates in real-time the average on 2, 4, 8 or 16 samples implementing a data decimation to minimise the file size of prolonged acquisitions. Averaged data are then transferred to the FIFO block. The data storage strategy is based on the use of a FIFO arranged by a dual layer stack memory with the first layer of 1k words (16 bit/word) which stores a pair header/data for each clock cycle at 20 MHz. The second layer is composed of 16k words and it is enabled only when the first FIFO stack is filled by three words. Header/data are then transferred at 20 MHz from the first layer to the second and then a *DATA\_READY* flag is sent to the USB interface.

When the flag is activated the computer software generates a *DATA\_TRANSFER* command which starts the transfer of the data from the second layer to the computer at 48 MHz through the USB link. This strategy is necessary because the USB link has a latency time between the *DATA\_READY* generated by the FIFO and the *DATA\_TRANSFER* command generated by the interface that is approximately 3 ms. This delay, corresponding to 6000 words, has to be compensated with a memory buffer size of 6k words at least. The Xilinx Spartan-3 consents to the use of 17 blocks of RAM to build a FIFO and the combination 1+16 blocks is the only one which maximises the buffer size allocable. This strategy allows a dynamic data storage to avoid data losses during the handshaking of the USB link. The USB link transfers the FIFO content to

the personal computer by blocks of 1064 byte; the graphical interface software (RadPlot) manages the number of blocks using a fixed virtual data buffer.

The CSU has also a trigger module (see Fig. 1) to manage external asynchronous triggers; this feature is particularly useful when the acquisition has to be synchronised with the Synchrotron Control System (based on SPEC [18]).

## 2.4 MRT Graphical User Interface - RadPlot

RadPlot is the graphical user interface (GUI) fully designed and developed at CMRP [19] specifically for synchrotron MRT and compiled under the C++ developing suite Nokia QT rev4.0. The GUI manages the USB link using dll (dynamic language library) specifically developed for the Cypress chip interface. It initializes the USB-link, sends the firmware to the FPGA by the USB-link and acknowledges if the device is connected and fully operating. At this stage, the GUI also manages all the controls and indicators for the hardware including the high voltage bias for the detector, the offset adjustment and the current samples of data acquired by the ADC.

Radplot is organized into two separate tabs for single triggering and multi-triggering data acquisition modes. The single trigger modality is used for the acquisition of the signal during a lateral scan of the sensor across the radiation field (dosimetry mode). The sensor is mounted on a linear stage motor (Newport UT100-150) with 0.1  $\mu$ m bidirectional accuracy and constant speed. The lateral scan motion is started prior to the trigger signal (*START* signal) to ensure a constant scanning speed is reached prior to the trigger signal being received. The trigger is generated by the Synchrotron Control System (SCS-SPEC) immediately before the main X-ray beam shutter is opened. Multi triggering modality is primarily used for alignment of the detector with the microbeams and enables the acquisition of a single (or user defined multiple) photoinduced current sample for each trigger pulse. RadPlot is fully platform independent and is supported by all the PC and MAC operating systems.

RadPlot immediately after a scan is able to complete a full set of statistical analysis of the microbeam array such as calculation of the PVDR, peak and valley position, peak and valley dose rate and peak FWHM identification. All the important features of the scan can be visualised within the data displayed at a reduced resolution compared to the written data file so as to speed up the visualization process. Analysis of the data is done post-scanning by the user with the only parameter requiring assistance from the user being the baseline signal identification.

# 3. Experimental results and discussion

Characterisation of the system has been carried out at the CMRP research laboratories and ESRF biomedical beam line (ID17). Electrical characterisation has been performed at CMRP to determine the gain, slew rate and noise performance. Experiments, carried out at ESRF, are reported to demonstrate the performance of the X-Tream system on synchrotron MRT. Relevant MRT X-ray beam parameters PVDR and spatial resolution have been determined and are discussed.

#### **3.1.1** System response characterization: Slew rate

Real-time dosimetric measurements in MRT are typically made in two ways. Both involve the translation of the dosimeter relative to the radiation field. This translation, combined with the very steep dose gradients associated with MRT places additional demands on the slew rate of the dosimetry system. The slew rate of a preamplifier, measured in  $V/\mu s$ , and is defined as the maximum rate of variation of the output voltage.

$$SR_{th} = \left|\frac{dV_{out}}{dt}\right|_{max}$$

Limitations of the slew rate can lead to a distortion of the shape of the measured output signal as a function of time. One of the main parameters in the characterization of the beam quality for MRT is each X-ray microbeam profile. To measure the microbeam profiles the X-Tream detector is moved at constant speed (typically 1 mm/sec) through the radiation field with a dose rate gradient of approximately 1000 Gy/sec/ $\mu$ m so it is crucial that the design of the preamplifier is such that the slew rate guarantees a minimum distortion in the measurement of the microbeam profile.

The theoretical slew rate necessary for a correct shaping of the MRT microbeams equals to 1.4  $mV/\mu s$  (see below) and its calculation is based on the following assumptions:

- Constant speed of the linear stage during the scan  $v_{stg} = 1mm/s$
- Sampling time of the signal is 1µs (sampling rate 1MHz)
- Correspondence of the distance d with time is:  $t = \frac{d}{v_{stg}}$
- Nominal microbeam shape modeled by a Monte Carlo simulation [21] with a width of 52µm and a c-t-c width of 420µm Fig.5(a) calculated at 10mm depth in water equivalent material.
- ADC input dynamic is 4.096 V and this voltage level represents the maximum variation possible from the signal generated by the detector and analog front-end within one clock sampling time.
- Calculation of the theoretical slew rate  $(SR_{th})$  for a voltage pulse with an amplitude of 4.096V corresponding to a microbeam peak at 10 mm depth in solid water is

$$SR_{th} = \max\left(\frac{dD}{dx}\right) = \frac{1.4V}{\mu m} \equiv \frac{1.4V}{ms} = \frac{1.4mV}{\mu s}$$

Fig.5(a) graphically shows how the calculation of the realistic slew rate expected in MRT was done. The left side axis of Fig.5(a) is the derivative of the expected signal from a microbeam based on the theoretical signal estimated by MC simulations (right side axis) at 10mm depth in solid water. To evaluate the slew rate we considered the scenario where the maximum of the microbeam peak corresponds to 4.096V (maximum amplitude of the input signal tolerated by the ADC) and the next sampling point is zero ADC units, corresponding to the worst case scenario in terms of variation of the signal.

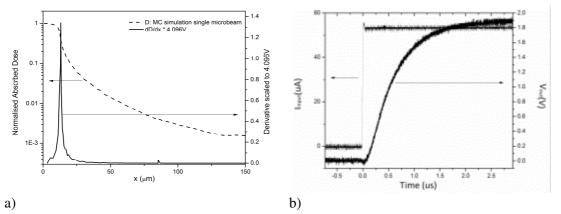


Fig.5: a) Calculation of a realistic slew rate expected in MRT. b) Experimental verification of the preamplifier/digital readout slew rate.

Fig.5(b) shows the experimental verification of the measured SSD sensor slew rate. A current square pulse of 50  $\mu$ A (left hand axis of Fig.5(b)) was used as an input to the transimpedance amplifier (TIA) and the corresponding output voltage signal was observed (right hand axis of Fig.5(b)) together on the digital oscilloscope. The dark grey trace represents the output voltage and it suggests a transimpedance gain of approximately  $2V/50\mu$ A  $\approx 10^4$  and a total slew rate SR<sub>exp</sub> =  $1.56 \text{ V}/\mu s \gg \text{SR}_{\text{th}}$ . The bandwidth of the analogue front end was also estimated to be approximately 520Hz with an equivalent input noise of  $0.83 \text{ } pA/\sqrt{Hz}$ . Tab.1 summarises the main parameters of the system.

Parameter	Description	Specification	Unit
Num. channel	Number of channel acquired	1	
Resolution	Analog to Digital conversion	16	Bit
Dynamic Range	Analog swing of the	80	dB
	preamplifier for positive and		
	negative input current		
Frequency Response	Lower/Upper cutoff	DC/520	Hz
EIN	Equivalent Input Noise	0.83	$pA/\sqrt{Hz}$
MIS	Maximum Input Signal @	~26	μA
	20kGy/s dose rate MRT		
	spectrum x-ray in silicon		
Input Bias Current	Input current offset	2	pA
MCR	Maximum conversion rate	1	MHz
MTR	Maximum Trigger Rate	1	MHz
Power consumption	Total power consumption	2	W
High Voltage range	Bias voltage range for the	±200	V
	detector		
Power Supply	X-Tream power supply	220	VAC

Tab.1: Summary of the specifications of X-Tream

#### 3.1.2 Conversion factor and electronics response linearity

The equivalent current to counts conversion factor has been measured using a constant current source from 4 nA to 20  $\mu$ A. The constant current source was used as the input of the preamplifier and the output was acquired by the DC level signal with the RadPlot software.

Fig.6 shows the linearity of the response of the system and ADC counts to nano-Ampere conversion factor was determined to be 2.51 counts/nA.

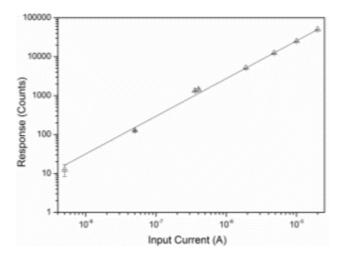


Fig.6: The current to counts conversion factor and response linearity as a function of the input DC current

#### 3.1.3 Noise performance

Evaluation of the dose rate in the valley between two adjacent X-ray microbeams is the most challenging scenario for the system in terms of sensitivity to small variations of the photocurrent generated in the detector above the baseline detector dark current. The noise corresponds to the fluctuation of the baseline and has been evaluated sampling the continuous current generated by the sensor in the dark and at room temperature.

When a continuous signal is sampled with a constant sampling rate the phenomenon of aliasing may occur. If  $f_s$  is the sampling rate, all the noise components at  $n \cdot f_s$  will appear as a DC offset of the signal. A shaper filter has been designed to cut off the bandwidth of the input signal of the ADC to  $f_s/2$ . The noise at the ADC input, using the redundant sampling rate of 1 MHz, has also been used to have a finer resolution than the Least Significant Bit (LSB) of the ADC. This technique, named dithering [20], is based on the use of sliding fixed width (N samples) windows to average the signal and reduce the noise impact by a factor  $N^{-1/2}$ .

The noise figure is therefore calculated by acquiring the baseline filtered by the shaper and then applying different averaging factors (depending on the speed of variation of the input signal) as reported in section 2.3. The distribution of the counts obtained by the acquisition of the baseline is matched by a Gaussian fit and the standard deviation of the fit is then considered the noise. Typical noise of X-Tream with the SSD sensor is approximately  $\pm 1.1$  counts (corresponding to  $\pm 0.43$ nA) with no averaging applied.

#### 3.2 Application of X-Tream in MRT: microbeam array measurement

The application of the X-Tream system using the dosimetry probe in MRT was recently demonstrated at the biomedical beamline (ID17) of the ESRF. The sensor was mounted so as to present the minimum possible cross section of the sensitive volume to the microbeams (i.e. end-on and edge-on orientation as shown in Fig.7(a)). Measurements were performed at depth of 6 cm on the central axis of a 15x15x15 cm<sup>3</sup> Perspex phantom, mounted on a computer controlled goniometer. Once precisely aligned using the multi-trigger DAQ mode, the detector was scanned through the microbeam array radiation field with the radiation induced detector current monitored by the X-Tream readout system operated in single trigger mode. A photograph of the experimental set up is shown in Fig.7(a) and a schematic top-view of the set up is shown in Fig.7b).

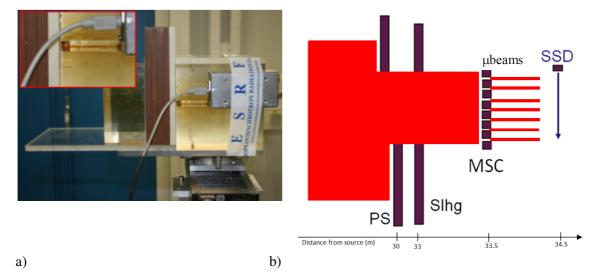


Fig.7: a) The Single Strip Detector (SSD) is positioned within the phantom in edge-on mode, on the goniometer. The linear stage controlled motor allows one to precisely move the detector across the microbeams at constant speed; inset is a zoom of the detector. b) Schematic top view representation of the main elements of the ID17 beamline; the primary slit collimator (PS) is followed by the Slit Horizontal Gap (Slhg) and then by the Multi Slit Collimator (MSC) which creates the microbeams.

All data along with other important parameters (motor positions, storage ring current etc) were logged at each detector position via a general purpose interface bus (GPIB), interfaced with the MRT control computer. The detector response can therefore, in principle, be corrected for the storage ring current at every point in a scan. However, in practice, this is only necessary from one scan to another as each detector lateral scan across the whole radiation field of approximately 35 mm requires approximately 35 seconds in total.

Fig.8(a) and (b) show a typical measured radiation field profile using the silicon sensor, and detail of the peak response respectively, prior to the insertion of the multislit collimator in the beam. The height of the X-ray beam was 50  $\mu$ m so as to minimize the dose delivered to the detector, which is approximately equal to the dimension of the sensitive volume of the detector in this direction. The profile uniformity is consistent with that expected from such a synchrotron source, and in agreement with Gafchromic film measurements [21]. The measured width of the

profile is in excellent agreement with preselected value set by the primary slits (as shown in Fig.7(b) and ultimately determines the number of X-ray microbeams. Prior to MSC insertion the primary slits can be adjusted so that the homogeneous profile is symmetric, although this was not done in these experiments. Insertion of the MSC leads to the striation of the homogeneous X-ray field.

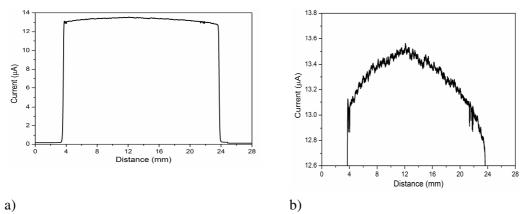


Fig.8: a) Homogeneous beam profile shaped by the primary slit collimator; b) zoom in of the profile for an estimation of the beam intensity uniformity

Fig.9(a) shows a typical profile of the microbeam array which includes 49 microbeams as measured by the SSD with a -30 V applied bias. The height of the X-ray field is 500  $\mu$ m in this case, which is the reason for the increase in the measured response (per mA of storage ring current) at the peaks of the microbeams compared to the homogeneous field plot in Fig.11a. Fluctuation of the measured response at the microbeam peak (Fig.9(b)) is observed to vary by significantly more than the fluctuations of intensity profile of the homogeneous beam. This is most likely due to the mechanical cutting process used to create the collimator slots in the MSC.

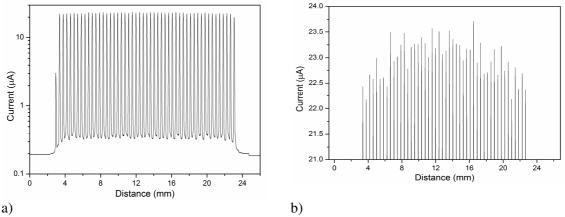


Fig.9: a) acquisition of 49 microbeams by a scan of approximately 10 seconds; b) zoom in of the variation of the peak amplitudes across the microbeams.

The statistics of the microbeam characteristics (FWHMs, PVDRs, microbeam peak and valley response etc) were deduced using the RadPlot analysis tool. The average FWHM of all microbeams was  $62\pm 2 \ \mu m$  (99% confidence limit). The distance between the peaks has been

also measured with an average value of  $410\pm3$  µm; although a larger spread of the accuracy occurs due to a longer range of movement of the linear stage and a consequent higher impact of vibrations and tiny misalignments, the value is in good agreement with the expected c-t-c distance of 412 µm.

Parameter	Description	Value
PVDR	Peak to Valley Dose Ratio	151±13
FWHM	Peak Full Width Half	62±2 μm
	Maximum	
PPD	Peak to Peak Distance	410±3 μm
N <sub>PEAK</sub>	Number of peaks	49
A <sub>PEAK</sub>	Average amplitude of peaks	57537±1404 counts or
		22.9±0.5 μA
A <sub>VALLEY</sub>	Average amplitude of valleys	377±14 counts or
		0.15±0.005 μA

Tab.2: On line data analysis of a microbeam scan test at 20mm depth in a PMMA phantom

The physical dimensions of each slot of the MLC is  $50\pm1$  µm with a centre-to-centre (c-t-c) spacing of the peaks of 400 µm. Divergence of the X-ray beam causes the c-t-c spacing to increases to 412 µm at the point of measurement (~1 m from the MSC). Ignoring the X-ray beam divergence (expected to add approximately one micron to the FWHM of each microbeam), the measured FWHM indicates that the effective spatial resolution (defined in this orientation of measurement, by the depletion length of the detector at -30V bias) of the detector is 10-12 µm. The effective spatial resolution for this sensor is defined by the trade-off between any detector misalignment and the depletion thickness. The guard ring electrode of the sensor design reduces the sensitive volume and the depletion thickness at this bias is therefore less than otherwise expected. This results shows the possibility to modulate the sensitive volume of the detector using the bias across the EPI layer and the opportunity to make the sensor even more spatially accurate reducing the thickness of the depleted region. Fig.9 clearly demonstrated the capability of the X-Tream system for real time and fast profiling of the X-ray microbeams. A full analysis of the dosimetric related details and parameters pertaining to MRT as measured by the sensor will be published elsewhere.

# 4. Conclusion

On-line and real-time dosimetry of intensive synchrotron microbeams is a major challenge. The Centre for Medical Radiation Physics has developed X-Tream, a quality assurance dosimetric system for clinical implementation of synchrotron X-ray microbeam radiation therapy, in collaboration with the research group of ESRF Medical Beam line ID17. X-Tream has the ability to measure the instantaneous MRT peak-to-valley dose ratio in solid water or water phantoms using a custom designed single strip silicon detector. Such measurements are needed to be made immediately prior to patient irradiation for verification of the patient treatment plan and treatment dose quality assurance check.

X-Tream is equipped with RadPlot, a graphical interface designed to control the system, manage the communication interface with the MRT control system (SPEC) and analyse the data

in real-time. An extensive characterization of the X-Tream system performance and characteristics has been carried out under full MRT treatment conditions at the ESRF and we have successfully measured the variation of the lateral response profile in a PMMA phantom. The beam parameter results are in agreement with previous independent measurements made by the ID17 team at ESRF.

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#### References

- R. Serduc, E. Bräuer-Krisch, A. Bouchet, L. Renaud, T. Brochard, A. Bravin, J. Laissue and G. Le Duc "First trial of spatial and temporal fractionations of the delivered dose using synchrotron microbeam radiation therapy" - J. Synchrotron Rad. 16, 587-590 (2009)
- [2] R. Serduc, A. Bouchet, E. Bräuer-Krisch, J. A Laissue, J. Spiga, S. Sarun, A. Bravin, C. Fonta, L. Renaud, J. Boutonnat, E. A. Siegbahn, F. Estève and G. Le Duc "Synchrotron microbeam radiation therapy for rat brain tumor palliation—influence of the microbeam width at constant valley dose" Phys. Med. Biol. 54 6711 (2009)
- [3] D.N. Slatkin et al. "Microbeam Radiation Therapy" Med. Phys. 19, 1355-1400 (1992)
- [4] E. Bräuer-Krisch et al., "MOSFET dosimetry for microbeam radiation therapy at the European Synchrotron Radiation Facility" Med. Phys. 30, 583 (2003)
- [5] E. Bräuer-Krisch, A. Bravin, L. Zhang, E. Siegbahn, J. Stepanek, H. Blattmann, D. N. Slatkin, J.O. Gebbers, M. Jasmin, and J. A. Laissue "Characterization of a tungsten/gas multislit collimator for microbeam radiation therapy at the European Synchrotron Radiation Facility" Rev. Sci. Instrum. 76, (2005)
- [6] E. Bräuer-Krisch, R. Serduc, E.A. Siegbahn, G. Le Duc, Y. Prezado, A. Bravin, H. Blattmann, J.A. Laissue "Effects of pulsed, spatially fractionated, microscopic synchrotron X-ray beams on normal and tumoral brain tissue" Mutation Research 704 (2010) 160–166
- [7] E. Bräuer-Krisch, A. Rosenfeld, M. Lerch, M. Petasecca, M. Akselrod, J. Sykora, J. Bartz, M. Ptaszkiewicz, P. Olko, A. Berg, M. Wieland, S. Doran, T. Brochard, A. Kamlowski, G. Cellere, A. Paccagnella, E. A. Siegbahn, Y. Prezado, I. Martinez-Rovira, A. Bravin, L. Dusseau, P. Berkvens "Potential High Resolution Dosimeters For MRT" 6th Intern. Conference on Medical Appl. Of Synch. Rad. AIP 978-0-7354-0813-5/10 (2010)
- [8] A. Rosenfeld, G. Kaplan, B. Allen, F. A. Dilmanian, T. Kron, and A. Holmes-Siedle, "MOSFET dosimetry of X-ray microbeams" IEEE Trans. Nucl Sci., vol. 46, no. 6, pp. 1774– 1780, (1999)
- [9] A. B.Rosenfeld, M. L. F. Lerch, T. Kron, E. Bräuer-Krisch, A. Bravin, A. Holmes-Siedle, and B. J. Allen, "Feasibility study of on-line, high spatial resolution MOSFET dosimetry in static and pulsed X-ray radiation fields" IEEE Trans. Nucl. Sci., vol. 48, no. 6, pp. 2061– 2068, (2001)

- [10] E. Bräuer-Krisch, A. Bravin, M. Lerch, A. B. Rosenfeld, J. Stepanek, M. DiMichiel, and J. A. Laissue, "MOSFET dosimetry for microbeam radiation therapy at the European synchrotron radiation facility" Med. Phys., vol. 30, no. 4, pp. 583–589, (2003)
- [11] A. B. Rosenfeld, E.A. Siegbahn, E. Brauer-Krish, A. Holmes-Siedle, M. L. F. Lerch, A. Bravin, I. M. Cornelius, G. J. Takacs, N. Painuly, H. Nettelback, T. Kron "Edge-on Face-to-Face MOSFET for Synchrotron Microbeam Dosimetry: MC Modeling" IEEE Trans. Nucl. Scie., Vol. 52, No. 6 (2005)
- [12] T. Kron, A.B. Rosenfeld, M.L.F. Lerch "Measurements in radiotherapy beams using online MOSFET detectors", Rad. Prot. Dos. 101 N1/4, 445-448 (2002)
- [13] Siegbahn et al. "MOSFET dosimetry in x -ray microbeams" 1129 Medical Physics, Vol. 36, No. 4 (2009)
- [14] A. Bravin "The biomedical programs at the ID17 beamline of the European Synchrotron Radiation Facility" Springer (2007)
- [15] Martínez-Rovir I., Prezado Y. "Monte Carlo dose enhancement studies in microbeam radiation therapy" Med Phys. 38(7), pp. 4430-9 (2011)
- [16] http://www.verilog.com/IEEEVerilog.html] and implemented by Xilinx ISE 9.2i
- [17] http://www.xilinx.com/products/design-tools/ise-design-suite/
- [18] http://www.certif.com/spec.html
- [19] Cullen et al. "Monte Carlo modelling of a silicon strip detector for microbeam radiation therapy" Radiation Measurements, Vol.46, Iss.12, pp. 1646–1649 (2011)
- [20] A. Oppenheim et al., "Signals and Systems", 2nd Ed. Upper Saddle River, NJ; Prentice-Hall, 1997
- [21] E.A. Siegbahn, E. Bräuer-Krisch, J. Stepanek, H. Blattmann, J.A. Laissue, A. Bravin "Dosimetric studies of microbeam radiation therapy (MRT) with Monte Carlo simulations" Nuclear Instruments and Methods in Physics Research A 548, 54–58 (2005)