behaviors by the Porsolt forced swim test, and locomotor activity and anxiety by the open field test. We also studied adult neurogenesis within the hippocampal dentate gyrus by using the thymidine analogue BrdU to label replicating stem cells. Ten months after irradiation animals were killed and brain tissue used for histology and immunohistochemistry.
Results: Microbeam irradiation did not alter cognitive performance. Interestingly, microbeam irradiation (300 Gy) significantly reduced the immobility time in the forced swim test without affecting locomotor activity as compared to control rats and 5-10 Gy irradiated rats. Histological analysis showed that microbeam irradiation did not alter the cytoarchitecture of the hippocampus with cell death observed only along the irradiation pathway. We did not observe a reduction of hippocampal neurogenesis, assessed by stereological counts of BrdU-positive cells in the dentate gyrus of the hippocampus at 10 months after microbeam irradiation.
Conclusions: These data shed light on the biological effects of microbeam irradiation on the CNS and may open new potential therapeutic strategies in cancer treatment and other CNS disorders.
Keywords: Microbeam radiation therapy, Hippocampus, Neurogenesis

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What are the Dominant Radiobiological Mechanisms at Play in Stereotactic Radiotherapy?
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Recent clinical results using Stereotactic Radiation Therapy (SRT) are very encouraging. Our goal is to investigate whether the excellent SRT tumor control data imply that there are new tumoricidal mechanisms that determine tumor control at high SRT doses – new mechanisms which are not present or have little effect at conventional radiotherapeutic doses.
To accomplish this, we investigate whether the standard LQ model with heterogeneity can provide as good a description of the SRT data as can models with extra terms describing unique high-dose tumor control mechanisms.
We analyzed published TCP data for lung tumors or brain metastases from 3000 SRT patients, covering a wide range of doses and fraction numbers. We used: (a) a linear-quadratic model (including heterogeneity), which assumes the same mechanisms at all doses, and (b) alternative models with terms describing distinct tumoricidal mechanisms at high doses.
Both for lung and brain data, the LQ model provided a significantly better fit over the entire range of treatment doses than did any of the models requiring extra terms at high doses. Analyzing the data as a function of fractionation (1 fraction *vs*. >1 fraction), there was no significant effect on TCP in the lung data, whereas for brain data multi-fraction SRT was associated with higher TCP than single-fraction treatment.
This analysis suggests that distinct tumoricidal mechanisms do not determine tumor control at high doses/fraction. Rather the excellent clinical outcomes seen with SRT are the result of the excellent dose distributions which SRT provides, which allow delivery of larger doses to the tumor than is possible with conventional radiotherapy. Finally, there is plausible evidence suggesting that multi-fraction SRT is superior to single-dose SRT.

Keywords: Stereotactic Radiotherapy Mechanisms

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GEANT4 simulation of dose deposition in patients from TomoTherapy Hi-Art Megavoltage computed tomography (MVCT) imaging.
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Purpose: Image-guided radiotherapy (IGRT) is a technique used to optimise RT beam delivery to the tumour by following its evolution over time through regular MVCT imaging of the treatment area.
However, its application is limited by clinical concerns over the additional dose coming from MVCT imaging, which we evaluate in this study.
Methods: We use the particle transport framework GEANT4[1] to model the X-ray beam line from the Tomotherapy Hi-Art RT treatment machine at the Addenbrooke's hospital and evaluate the imaging dose delivered to the vicinity of the tumour. Dose maps are obtained by combining simulations of the CT scan using a static beam line with 51 different exposition angles.
All GEANT4 simulations were performed on UK grid resources[2] to maximize parallel throughput, using anonymised data.
Results: Simulated beam profiles (PDD, longitudinal and lateral) with different MLC beam patterns were compared to actual calibration data taken in water tank at Addenbrooke's hospital. The agreement between the model and the calibration is quantified by the Gamma index[3]. Less than 2% of the simulated points exceed Gamma(1%,1mm)
We also simulated the imaging dose distribution in a prostate patient treated in 34 fractions, each fraction starting with one MV CT used for image guidance. We used a fan beam width of 4 mm with a pitch of 2 mm. The results are shown in Figure 1.

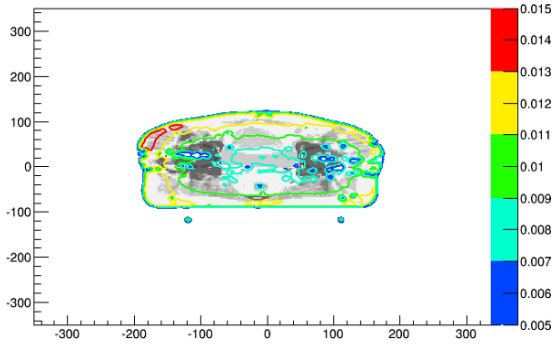

Figure 1: Normalised imaging dose distributions in Gy for a prostate cancer patient, in a transverse plane in the treatment region.

The maximum simulated dose is about 1.5 cGy on a single MVCT, in agreement with results found in [4] using proprietary software. For comparison, the treatment dose in the same area goes up to 2 Gy per fraction.
Conclusions: We have successfully modeled the Megavoltage imaging beam line of the Tomotherapy Hi-Art machine used for radiotherapy at the Addenbrooke's hospital using Geant 4 and used it to derive dose maps in the patient.
Doses were found to be in agreement with other published results and negligible with respect to the treatment dose.

Keywords: MVCT, dose, Monte-Carlo, Geant4

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Recurrent glioblastoma multiforme – targeted alpha therapy with ^{213}Bi-DOTA-Substance P

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Glioblastoma multiforme (GBM) is the most common and malignant primary brain tumor. The median survival time is 14.6 months from time of diagnosis, in spite of aggressive surgery, radiation therapy and chemotherapy. Only 3 to 5% of patients survive more than three years. Recurrence of GBM is nearly universal, confers a dismal prognosis with a 6-months progression free survival (6M-PFS) rate of 15% to 21% and a median survival of 6.2 months. Advancements in the past decades have not significantly increased the overall survival of patients with this disease. GBM has been demonstrated NK-1 receptor system and Substance P can be used as a ligand for targeted therapy. Alpha emitter, like ^{213}Bi offers the new potential for selective irradiation of tumors, with minimizing damage to adjacent tissue.
Material and methods: 21 patients with primary recurrent glia tumor IV after standard therapy were included in the study during two years. Following intracavitary or intratumoral insertion of 1-2 catheter systems, patients were treated with 1–8 doses of 2 GBq ^{213}Bi-DOTA-Substance P (^{213}Bi-SP) in intervals of 2 months. ^{68}Ga-DOTA-Substance P (^{68}Ga-SP) was co-injected with the therapeutic doses to assess biodistribution using PET/CT. Therapeutic response was monitored with MRI. Study was approved by the ethical committee of the Medical University of Warsaw.
Results: Treatment with activity up to 13 GBq ^{213}Bi-SP was tolerated well with only mild transient adverse reactions: in 1 patient transient increase of focal neurological symptoms and in 3 patients episodes of epileptic seizures several days after treatment. PET/CT imaging showed high retention of the radiolabeled peptide at the tumor site.
Out of 21 evaluable patients, 17 progressed within the follow-up period, 5 of them are alive at the end of follow-up. Four patients were excluded from evaluation due to lack of data. Median progression free survival was 3.7 months, with a 6 months progression free survival rate of 19% . The median overall survival from the first diagnosis was 25.2 months, and from the start of ^{213}Bi-SP was 6.5 months. Follow up of therapeutic responses and toxicity is continued and patient recruitment is ongoing. Busk

Conclusions: Treatment of recurrent GBM with ^{213}Bi-SP is safe and well tolerated. Targeted alpha therapy with ^{213}Bi-SP may evolve as a promising novel option for treatment of recurrent GBM.

Keywords:targeted alpha therapy; ^{213}Bi-DOTA-Substance P; glioblastoma multiforme

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Increasing PET scanner resolution using a Silicon detector probe

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A high-resolution silicon detector probe, in coincidence with a conventional
PET scanner, is expected to provide images of higher spatial resolution than those achievable using the scanner alone, due to the finer pixelization of the probe detector[1]. A PET-probe prototype is being developed utilizing this principle [2]. The system includes a probe consisting of ten layers of silicon detectors, each a 80×52 array of 1×1×1 mm^3 pixels, to be operated in coincidence with a modern clinical PET scanner. Detailed simulation studies of this system have been performed to assess the effect of the additional probe information on the quality of the reconstructed images.
Using the Monte-Carlo simulation package GATE, a grid of point sources was simulated to study the contribution of the probe to the system resolution at different locations over the field of view (FOV). A resolution phantom was used to demonstrate the effect on image resolution for two probe positions. A homogeneous source distribution with hot and cold regions was used to demonstrate that the localized improvement in resolution does not come at the expense of the overall quality of the image. An imaging study using experimental probe data was also performed. The list-mode maximum likelihood–expectation maximization (ML–EM) algorithm[3] was used for image reconstruction in all cases.
As expected, the point spread function of the PET-probe system was found to be non-isotropic and vary with position, offering improvement in specific regions. An increase in resolution, of factors of up to 2, was observed in the region close to the probe. Images of the resolution phantom showed visible enhancement in resolution when including the probe in the simulations, as can be seen in figure 1. The image quality study demonstrated that contrast and spill-over ratio in other areas of the FOV were not sacrificed for this enhancement. The improvement in resolution when using the Si detector probe was also observed using the experimental prototype. In this context, previously unrecoverable features in a resolution phantom could be resolved when probe data was included during image reconstruction. Remaining challenges in developing the PET-probe system include overcoming the limitations imposed by the timing performance of the Si detectors and more detailed system modeling in image reconstruction.

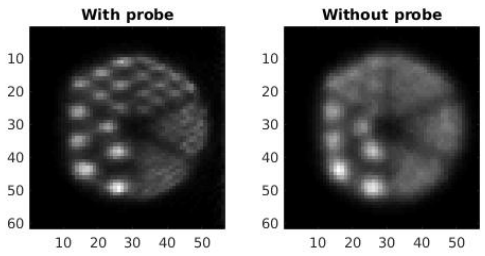

Figure 1: Images of the resolution phantom reconstructed using data from the probe and from the scanner alone. The probe is located to the right of the image, in close proximity to the phantom. The phantom features are 4.8, 4.0, 3.2, 2.4, 1.6 and 1.2 mm in diameter. Pixels are 1 × 1 × 1 mm3

Keywords: PET, Si detectors, PET insert

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