to their ease of isolation and manipulation, and wound/tumour homing capacity. HAMSCs have been successfully used in suicide gene therapy, employing the prodrug activating system based on Herpes simplex virus type I thymidine kinase (HSV-TK)/ganciclovir (GCV). In the current study we demonstrate an effective model of glioblastoma therapy based on the use of genetically modified hAMSCs and *in vivo* monitoring of tumour and therapeutic cells.
Methods: Bioluminescence imaging (BLI) of cells expressing different luciferases allows the simultaneous monitoring of different cell populations, cell distribution, proliferation or differentiation. We stably transduced hAMSCs for expression of *Renilla* luciferase, HSV-TK and red fluorescent protein, generating RLuc-R-TK-AMSC and U87MG human malignant glioma cells for expression of *Firefly* luciferase and green fluorescent protein, generating Pluc-G-U87 cells. SCID mice were stereotactically implanted in the brain with Pluc-G-U87 and RLuc-R-TK-AMSC cells and subjected to GCV treatment. Tumour response was monitored in vivo by bioluminiscence imaging. Therapeutic cell differentiation was assessed by labeling the above *Renilla* luciferase expressing hAMSCs with a *Firefly* luciferase reporter regulated by the CD31, endothelial specific, promoter and *in vivo* monitorization.
Results: Continuous monitoring of tumour size by BLI showed that hAMSCs/GCV treatment resulted in a significant reduction (99.9% vs. control) of tumour cell number. In addition, the combination of BLI and confocal microscopy analysis of therapeutic cells suggests that efficient tumour eradication results from hAMSCs homing to tumour vessels, where they differentiate to endothelial cells, intensifying their cytotoxic effect by destroying tumour vasculature and negating nutrient supply.
Conclusion: We propose that genetically modified hAMSCs can be useful vehicles in clinical applications to deliver localized therapy to glioma surgical borders after tumour resection.

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Diffuse Reflectance Spectroscopy as an Optical Guidance Tool for Breast Biopsies

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Background: During diffuse reflectance spectroscopy (DRS), tissue is illuminated by a broadband white light. Subsequent alterations in the light spectrum occur due to scattering and absorption. Specific quantitative biochemical and morphological information from the examined tissue can be derived from spectral changes and provide information on cellular metabolic rate, vascularity, intra-vascular oxygenation and alterations in tissue morphology. Thus, DRS allows specific differentiation between tissues by differences on molecular and morphological level and has the potential to be incorporated into optical tools for cancer diagnosis and therapy. We hypothesize that an individualised approach in breast tissue analysis will improve discrimination accuracy for a DRS optical biopsy guidance tool.
Methods: DRS was performed on excised normal and malignant breast tissue from 24 female breast cancer patients. Tissue samples from macroscopic normal adipose tissue, glandular tissue, Ductal Carcinoma in situ (DCIS) and invasive carcinoma were included in the optical analysis. Optical spectra were collected over a wavelength range from 500 to 1600 nm. Model based data analysis was performed on the collected tissue spectra from all patients collectively and each patient individually. Results were compared to histology analysis.
Results: A total of 555 spectra were collected from 115 tissue locations in the mastectomy specimen. Six patients were diagnosed with DCIS, 16 patients had an invasive carcinoma and 2 patients had both DCIS and an invasive carcinoma. The classification accuracy of the data from all patients divided into two groups (*normal breast tissue* and *malignant tissue*) was achieved with a sensitivity and specificity of respectively 90% and 95%. The overall classification accuracy was 93%.
Classification of the data was also performed for each patient individually. Individualised approach yielded a 100% discrimination accuracy between normal and malignant breast tissue for 20 of the 24 patients.
Conclusion: DRS is able to discriminate malignant breast tissue from normal breast tissue with high accuracy. A 93% discriminative accuracy in an overall analysis was further enhanced to 100% for most of the included patients in an individual analysis. These results support further validation of this method during *in-vivo* studies, and eventually the application of DRS in minimal invasive tools (biopsy needles). A feasibility study in the clinical setting has been initiated.

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Tissue Composition Estimated With an Interventional Fiber Optic Probe During Liver Tissue Resection

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Background: In the field of surgical and interventional oncology, it is of major importance to know where to excise tumorous tissue and to exactly assess its margins. A new development renders tissue characterization of tissue possible through the use of fiber optic probes and optical spectroscopy. These spectroscopic measurements are translated into clinically relevant physiological parameters and can be used to discriminate tumours from healthy tissue.
Material and Methods: Optical measurements were collected with a custom-made optical probe that comprises an optical fiber connected to a light source and two other fibers connected to detectors that resolve light from 500 to 1600 nm. The measured signals correspond to diffuse reflectance spectra from which the various physiological and morphological parameters of interest are derived by fitting an analytical model to the measurements. In total, 14 samples that underwent partial liver hepatectomy were measured and 230 spectra were collected at the tumour sites and 212 spectra at the normal tissue surrounding the tumour. From the tissue optical properties derived from the fitting model, biological concentrations are derived such as blood, water, lipid and bile volume fractions as well as morphological parameters such as the scattering of light in tissue correlated to tissue density. Kruskal-Wallis statistical test is applied to the data to investigate which tissue parameters demonstrate significance difference between tumours and healthy tissue ($P < 0.01$).
Results: Medians and corresponding standard deviations were computed for the parameters derived from the measurements acquired within the 14 samples of each tissue category. After application of the Kruskal-Wallis statistical test, the bile and water volume fractions as well as the reduced scattering amplitude showed significant differences as summarized in the table.

	Healthy liver (14 samples)	Tumours (14 samples)	*P*-value
Bile (%)	5.5±2.3	1.0±1.1	0.00005
Water (%)	76±4	93±17	0.005
Scattering amplitude (cm^{-1})	17±3	10±3	0.00001

Conclusions: Diffuse optical spectroscopy enables discrimination between metastatic tumours and healthy liver tissue based on the bile and water volume fractions as well as the reduced scattering amplitude. Hence, optical sensing at the tip of a probe has an interesting potential for tumour margin assessment during liver resection.

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Feasibility of Boosting Local Dose to Tumour Endothelial Cells Using Vascular-targeted Bismuth Nanoparticles During Radiotherapy

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Background: The use of coated bismuth nanoparticles (BiNs) and their bioconjugates has recently been shown for enhanced *in vivo* imaging of the vasculature in mice, with high x-ray contrast mainly due to photo-electric absorption. In this study the dosimetric potential of exploiting this photo-electric effect to significantly boost local dose to tumour endothelial cells (ECs) during radiotherapy is examined.
Methods: A tumour vascular endothelial cell (EC) is modeled as a slab of 2 μm (thickness) × 10 μm (length) × 10 μm (width). Analytic calculations based on the electron energy loss formula of Cole were carried out to estimate the dose enhancement from photoelectrons to the EC from BiNs attached to the exterior surface of the EC. The endothelial dose enhancement factor (EDEF), representing the ratio of the dose to the EC with and without nanoparticles was calculated for different nanoparticle concentrations. The investigated concentration range considers the non-uniform distribution of nanoparticles, with significantly higher local concentration expected near the EC. Five radiotherapy sources