

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 bioluminescence 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* monitoring.

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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ORAL

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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ORAL

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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ORAL

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

were investigated, Pd-103, I-125, Yb-169, 50kVp x-rays, and 6 MV x-rays. The results are compared to recently published data calculated with the same approach when using gold nanoparticles.

Results: For BiN concentrations ranging from 7–140 mg/g, EDEF values of 1.33–7.52, 1.31–7.25, 1.04–1.84, 1.27–6.48, and 1.28–6.67, were calculated for Pd-103, I-125, Yb-169, 50 kVp, and 6 MV, respectively. Apart from the results for Pd-103, the calculated EDEFs predict higher dose enhancement due to photo-electrons when using BiNs as compared to when using gold nanoparticles.

Conclusions: The results predict that significant dose enhancement to tumour endothelial cells may be achieved by applying tumour vasculature-targeted BiNs as adjuvants to radiotherapy. BiNs may provide a low cost alternative to the potential use of gold nanoparticles for vascular dose painting or as radiosensitizers during radiotherapy.

Table: Endothelial dose enhancement due to photo electrons for various radiotherapy sources

	EDEF due to photoelectrons from					
	Bismuth nanoparticles			Gold nanoparticles		
	7 mg/g	30 mg/g	140 mg/g	7 mg/g	30 mg/g	140 mg/g
Pd-103	1.33	3.00	7.52	1.42	2.81	9.46
I-125	1.31	2.34	7.25	1.26	2.10	6.12
Yb-169	1.04	1.18	1.84	1.03	1.15	1.68
50 kVp	1.27	2.17	6.48	1.25	2.08	6.05
6 MV	1.28	2.21	6.67	1.20	1.70	4.4

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ORAL

Impact of Electronic Treatment Scheduling and Web Based Communication Technology on Systemic Therapy Delivery at the Sunnybrook Odette Cancer Center, Toronto, Canada

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Background: The Odette Cancer Centre (OCC) is the sixth largest cancer institution in North America and currently manages over 18,000 chemotherapy patient visits per year. Current barriers to efficient and effective delivery of chemotherapy included scheduling inefficiencies and staff communication. These issues were addressed via two distinct mechanisms: (1) chemotherapy scheduling tool and (2) electronic communication tool for nurses and pharmacy staff.

Methods: An electronic Chemotherapy Appointment Reservation Manager (CHARM) was developed in house. CHARM is configured to calculate treatment times based on the pharmacist chemotherapy prep, nursing time and time for drug administration. In addition a new electronic web based communication tool was developed and implemented to facilitate communication between nursing and pharmacy staff. Data were prospectively collected for 2-week intervals in both 2009 and 2010 to assess the effect of both new programs. A flow-time analysis, patient and staff satisfaction surveys were conducted comparing the two time frames.

Results: For 2009, data was collected for 381 of 796 total patients treated in the two-week period (47.9%). For 2010, data was collected for 602 of 836 total patients. An increase in year-to-year volume of 5% was noted.

Thirty-six percent of patients started chemotherapy +/- 30 min of their scheduled time in both 2009 and 2010. However, the number of patients treated >30 mins after their scheduled appointments increased from 68 (20.7%) to 357 (71.1%). Patients receiving treatment in the correct bed assignment decreased from 45% in 2009 to 30% in 2010.

The distribution of patient arrival times was skewed with 58.1% of patients scheduled to arrive prior to 10am, 23.4% between 10–12 and only 18.4% after 12. In 2010, 69.3% of patients arrived earlier than their scheduled appointment by more than 30 minutes, with a mean arrival time of 117 minutes earlier than scheduled. Seven percent of patients arrived greater than 30 minutes late, with a mean arrival time of 49 mins late.

Time from patient registration on arrival to:	2009 (min)	2010 (min)
Patient on chemotherapy unit	33	43
Nursing approval for administration	80	85
Pharmacy approval of administration	89	94
Patient arrival in chemotherapy chair	110	137
Chemotherapy prepared	114	132
Initiation of chemotherapy	125	173

In 2010, a reduction in phone calls (for chemotherapy approval) between the nurses and pharmacy of 89% was observed. The number of chemotherapy order clarifications was similarly reduced by 91%. Nurses were more likely to agree or strongly agree that communication positively impacted on chemotherapy administration after implementation of the communication tool (80% vs. 37%).

Conclusions: Despite the implementation of CHARM, there was little change in patient flow. Possible explanations include increased patient volumes without infrastructure increases and suboptimal patient arrival patterns. To realize the full potential of the new reservation management system, adherence and redistribution of scheduled appointment times will be necessary along with proper chair placement. The online communication tool has resulted in improved flow in the chemotherapy unit as well as increased nursing satisfaction.

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ORAL

Survey of UK Cancer Patients, Exploring Their Internet Usage and Potential for Text Messaging Communication With Their Hospital

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Background: The aim of the survey was to explore cancer patients' use of the internet and elicit their opinion regarding communication with the hospital via electronic methods.

Methods: A questionnaire was developed consisting of four questions:

1. Do you (or a carer) access the internet?
2. Would you (or a carer) be prepared to enter details about your side effects from treatment through a dedicated and secure website?
3. Do you (or a carer) have/use a mobile telephone, specifically to send/receive text messages?
4. Would you (or a carer) be prepared to allow the hospital to send you text messages relating to your treatment?

Data was collected from 445 patients attending Northampton General Hospital for chemotherapy and/or radiotherapy during February 2011 – both by direct questioning & paper questionnaire.

Results: Answers to questions:

- Q1. 322 (72%) patients have access to the internet.
 Q2. 296 (67%) of those questioned would be prepared to record toxicities via website (92% of those who access the internet).
 Q3. 351 (79%) have or use a mobile phone for accessing text messages.
 Q4. 326 (73%) would be prepared to allow our hospital to communicate via text messages with regard to their treatment (93% of those with mobile phones).

Data relating to variation with age shows that up to 70 years old the majority of our patients (up to 85% in those patients in their 4th decade) would be willing to use these types of technology to communicate with our hospital. In those aged over 70 this proportion falls but is still >40%.

Conclusions: This study supports the hypothesis that UK patients support the introduction of electronic communications between a hospital and oncology patients receiving treatment. Under 70 years old the majority of individuals supported the use of both types of communication. Those over 70 years old were less enthusiastic but were more in favour of the use of text messages than the internet. We believe that the introduction of an electronic system to communicate with our patients, via the internet and/or text messaging, would enhance the patient's experience adding support to this type of initiative.

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ORAL

Tele Oncology Clinics in Rural Australia: a Cost-effective Cancer Care Model

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Background: Cost benefit studies in telemedicine are often incomplete and compare establishment costs with outpatient costs only. While some studies reported marginal benefit, others found no savings. We conducted a comprehensive cost benefit analysis of tele oncology clinics at Townsville Cancer Centre (TCC) and its rural centres in North Queensland, Australia.

Methods: Data on teleoncology clinics between March 2007 and November 2010 was gathered from the Oncology Information Management system. Patient travel expense information was provided by the QLD Health patient travel office. A model proposed by Dr B L Crowe (Health Informatics Society of Australia) was used for the calculation. Factors used are shown in the table.