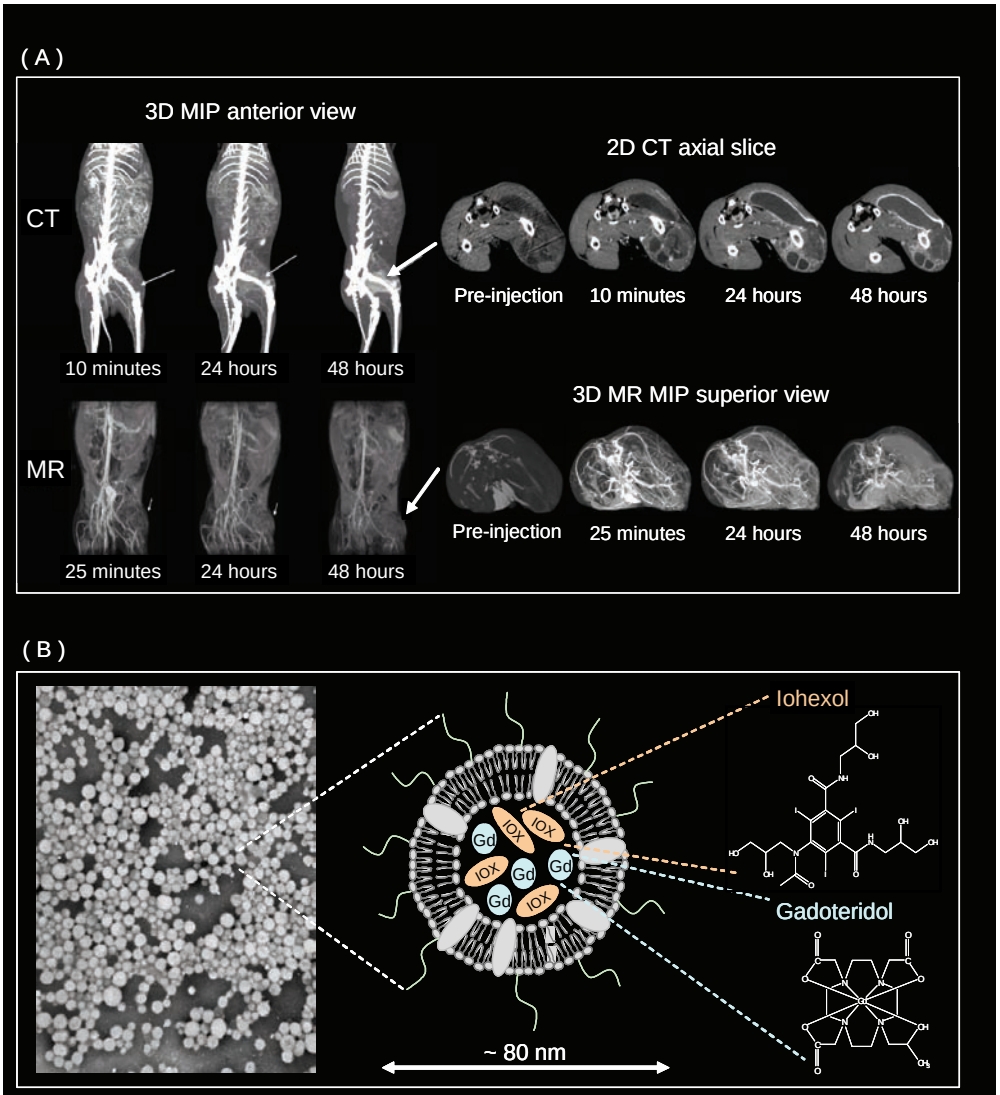
InterACTIONS

CANADIAN MEDICAL PHYSICS NEWSLETTER
Le BULLETIN CANADIEN de PHYSIQUE MÉDICALE



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53 (4) octobre/October 2007

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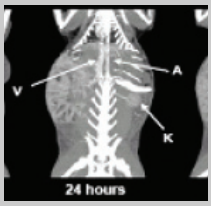
InterACTIONS

Volume 53, Number 4– octobre/October 2007



Cover Image

A collaborative project between the Radiation Medicine Program at the Princess Margaret Hospital in Toronto and the Faculty of Pharmaceutical Sciences at the University of Toronto has resulted in the successful development of a nanoparticulate contrast agent platform that supports multimodality imaging in CT and MR (Figure A). This nano-system consists of liposomes, which are the most established of the advanced drug delivery vehicles, that co-encapsulate two conventional small molecular weight contrast agents, iohexol (Omnipaque®), an iodine-based CT agent, and gadoteridol (Prohance®), a gadolinium-based MR agent (Figure B).

This liposome-based system is able to provide simultaneous and co-localized contrast enhancement that is detectable for days *in vivo* in two distinct imaging modalities. Due to its critical size (~ 80 nm) and high molecular weight, its distribution is confined within healthy blood vessels following intravenous administration. As a result, its slow clearance from the systemic circulation makes it valuable for longitudinal imaging applications. Its vascular circulation half-life is ~20 hours in mice and ~100 hours in rabbits. In the presence of vascular abnormalities, such as tumor vessels with enhanced permeability, this liposome-based agent leaks into the tumor interstitium, allowing for localization of angiogenic vasculature. Current investigations are focused on the characterization of the enhanced permeation and retention effect of liposomes at tumor sites and to correlate this effect with regional micro-vessel density and permeability.

Figure A: 3D maximum intensity projections (MIP) and 2D axial views of a VX2 sarcoma bearing New Zealand White rabbit (3 kg) imaged in CT (GE Discovery ST, 120 kVp and 200 mA) and MR (1.5 T GE Signa TwinSpeed and a head coil, 3D FSPGR, TR/TE = 9.8/4.3) following a single injection of the liposome agent (340 mg/kg of iodine and 20 mg/kg of gadolinium). Figure B: transmission electron micrograph (75 kV) of negatively strained liposomes and illustration of its composition.

Image provided by Jinzi Zheng, Christine Allen and David A. Jaffray, University of Toronto

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Please submit stories in Publisher 98, Word 6.0, Word 97, or ASCII text format. Hardcopy submissions will be scanned to generate an electronic document for inclusion in the Newsletter. Images in Tiff format at 300 dpi resolution are preferred.

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Message from the COMP Chair:

This summer has been a busy one for the organizing committee of this years' joint COMP/CARO meeting. I would like to thank the organizing committee and the many volunteers helping to make this event a success. In particular, I'd like to thank Peter O'Brien, Jean-Pierre Bissonnette, Nancy Barrett and Gisele Kite for the time and effort that they have put into making this a historic meeting.

As far as I am aware this will be the first time that COMP and CARO have met together, without any other organizations involvement. I would also like to express my appreciation to the anonymous COMP members who reviewed numerous articles for the Sylvia Fedoruk Award and to the Medal Committee, chaired by David Rogers, who reviewed the nominations for the Gold Medal award.

The Image Guided and Adaptive Radiation Therapy theme of this conference is very topical and if the number of submitted abstracts is anything to go by, there is a huge interest in the meeting.

In designing the scientific program, there has been a concerted effort by the organizing committee to promote interdisciplinary education and to make the varied and interesting sessions and workshops accessible to members of both COMP and CARO.

The Image Guided and Adaptive Radiation Therapy theme of this conference is very topical and if the number of submitted abstracts is anything to go by, there is a huge interest in the meeting. However, any joint venture has its challenges and this meeting is no exception.

To offset the limited time available for oral presentations, the number of poster slots has been significantly increased over what we normally have, but even so, we were only able to accept about 70% of the submitted abstracts because of time/space constraints.

The joint nature of the Resident/ Young Investigators Symposium has also limited the number of COMP students we could select, but all the talks look extremely interesting and I have no doubt that they will be of the high quality normally associated with our Young Investigators Symposium.

All abstracts were reviewed, in a blind fashion, by a dedicated group of COMP and CARO members and the proffered papers contain, in my view, an excellent mix of topics with equitable representation from both organizations and most parts of the country.

In this vein, COMP's Public Lecture will be given by a cancer survivor and a speaker who is trained both as a physicist and as a radiation oncologist while the CARO Lecture will be given by a physicist.

We have had a number of successful meetings with other organizations in the past and COMP is committed to continuing such collaborative efforts where it is in the interests of its members.

Our strategic planning exercise, which you will hear more about at the AGM, highlighted the need to work more closely with other organizations and joint meetings are one way of doing so.

However, we have also committed to ensuring that the flavor and intimacy of the stand-alone COMP meetings are not lost and so we will continue to hold these at least every second year.

Dr. Stephen Pistorius
COMP President

As far as I am aware this will be the first time that COMP and CARO have met together, without any other organizations involvement.

One such meeting will be held in 2008 and the Local Arrangements Committee under the leadership of Luc Beaulieu is already hard at work preparing for our meeting at the Université Laval.

The first announcements should have reached you by the time this is published and so while you are preparing to attend the joint COMP/CARO meeting in Toronto please do not forget to mark your calendars for the June 25-28, 2008 meeting where we can help celebrate Québec's 400th anniversary.

Message from the CCPM President:

This issue of InterACTIONS has a report from Peter Dunscombe, one of two CCPM representatives on the CAMPEP board (Ervin Podgorsak is the 2nd).

The report describes the issue of ABR requiring that by 2012 candidates sitting for their ABR certification exam must have graduated from a CAMPEP approved medical physics training program.

For those not familiar with CAMPEP, the Committee on Accreditation of Medical Physics Educational Programs is sponsored by the AAPM, ABR, ACMP, and the CCPM and accredits training programs in both therapy and imaging medical physics.

Currently 13 medical physics graduate programs are accredited, 4 of them in Canada (McGill, U of Calgary – Tom Baker Cancer Centre, UBC, and U of Alberta – Cross Cancer Institute, and 13 residency training programs are accredited, 3 of them in Canada (McGill, U of Calgary – TBCC, and the U of Alberta – CCI).

The residency program at the U. of Alberta is accredited in both therapy and imaging.

Although this is not yet an official ABR requirement, Peter Dunscombe's report suggests that some form of this requirement will be implemented by the ABR in 2012.

The concern is that CCPM certification will no longer be recognized in the USA unless the CCPM implements the same requirement: beginning in 2012 only graduates from a CAMPEP accredited training program will be eligible for CCPM board certification.

This issue will be open for discussion at the CCPM AGM in Toronto this October.

Dr. Dick Drost,
CCPM President

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The concern is that CCPM certification will no longer be recognized in the USA unless the CCPM implements the same requirement

Message from the Executive Director of COMP/CCPM:

I am sure you all agree that time certainly flies! I hope you had an enjoyable summer and are able to take some time to appreciate the beauty of the fall season.

COMP/CARO Conference in Toronto
Collaborating with CARO to conduct this conference has indeed been an enriching experience. We look forward to receiving your feedback on how the conference supported your needs for education and networking opportunities. This feedback is important to us as we continue to plan future events.

Other Conferences
Although we are just finishing our 2007 conference, Luc Beaulieu and his team are working hard on the 2008 Annual Scientific Meeting which will be taking place in beautiful and historic Quebec City. The dates have been set for June 25-28 so mark you calendars! As of this writing, we are still looking for a host city for 2009. Perhaps you and your colleagues would like to showcase your team and your city? A Request for Proposal can be found in this newsletter and provides further details.

A new website will support our efforts to communicate internally with our members and also externally as we work to promote the profession of medical physics to prospective members, legislators and the public at large

COMP Website

In the July issue of InterACTIONS, I mentioned that as part of our overall communication strategy we are revamping the COMP website. A new website will support our efforts to communicate internally with our members and also externally as we work to promote the profession of medical physics to prospective members, legislators and the public at large.

A Request for Proposal was circulated to prospective proponents who have specific experience providing services to scientific/medical associations and Darcy Mason, Boyd McCurdy Gavin Cranmer-Sargison and I evaluated the proposals and met via teleconference with the companies on the short list.

Our corporate members continue to support us very generously through advertisements and by exhibiting and sponsoring our annual conference.

We are happy to report that we have selected 4Poyntz Dezign Inc. to help us with this project. Development has begun on the new site which will be launched in November 2007 and we will keep you informed as changes occur. Stay tuned and feel free to share any feedback you might have as we progress!

COMP Finance and Administration

As per the direction given to us at the 2006 Annual General Meeting, we developed an RFP for audit services for the 2006 financial year. We hired the accounting firm, Nephin Winter to conduct the 2006 financial audit. Maryse Mondat and Gisele Kite put considerable time into preparing the documentation for this audit and centralizing the COMP finances so that our office is now handling the day-to-day financial management using standard accounting practices. This change frees up the COMP Treasurer to develop financial management strategies and to continue to oversee the financial health of the organization.

Ms. Nancy Barrett,
COMP/CCPM Executive Director

Corporate Member Support
Our corporate members continue to support us very generously through advertisements and by exhibiting and sponsoring our annual conference. This is an important source of non-dues revenue that supports our activities and we are grateful for this contribution.

Both Gisele and I thank you for your support and look forward to continuing to work with the COMP Executive and CCPM Board to address your priorities.

As always I welcome your feedback and suggestions.

Please feel free to contact me at nancy@medphys.ca or Gisele at admin@medphys.ca at any time.

2007 CCPM Chief Examiners Report

Submitted by: Michael Evans
McGill University Hospital, Montreal, QC

In January 2007, 51 MCCPM and FCCPM candidates passed credential review and their names were forwarded by the CCPM Registrar for the exam process.

The MCCPM written exam took place on Saturday March 10 in Vancouver, Edmonton, Calgary, Winnipeg, Toronto, Ottawa, Montreal, Moncton and Sydney.

There were 29 candidates (26 Radiation Oncology, 2 MRI, 1 Diagnostic). This was the first year that the Radiation Oncology specialty exam with the new format for Parts III and IV was used.

Of the 29 candidates writing the exam, 22 passed.

The Radiation Oncology oral exams took place in Montreal in May at the McGill University Medical Simulation Centre, and the MRI and Diagnostic oral exams took place in Toronto at Sunnybrook Hospital in July. There were 26 candidates for oral exams, including the 22 that passed the written exam in 2007, and 4 oral candidates that returned from 2006.

Of these 26 candidates, 23 were successful.

The following 23 candidates have passed the written and oral components of the MCCPM exam:

Syed Abbas,
Deidre Batchelar,
James Beck,
Akbar Beiki-Ardakani,
Jason Belec,
Anita Berndt,
Timothy Craig,
Idris Elbakri,
David Goodyear,
Fadi Hobeila,
Deborah Hodefi,
Rao Kahn,
Li Heng Liang,
Geetha Menon,
Sylvain Nadeau,
Keith Nakonechny,
Thomas Purdie,
Martin Shim,
Alasdair Syme,
Nada Tomic,
Keith Wachowicz,
Yizhen Wang,
Brad Warkentin.

Congratulations on this achievement! In the tradition of the CCPM, these candidates' election to Membership in the Canadian College of Physicists in Medicine will be ratified at the next annual general meeting, to be held in Toronto in October.

This year the CCPM Fellowship exams will be held October 9 and 10 in Toronto during the joint COMP/CARO conference. Results of these FCCPM exams will be reported on in a later newsletter. Currently there are 13 FCCPM candidates; 12 candidates in Radiation Oncology and 1 candidate in Nuclear Medicine.

This was my first year as Chief Examiner (somehow the promotion from Deputy Chief could not be avoided…), and I would like to thank the many people who have helped me. It is quite obvious that the CCPM could not run without the commitment and interest of its members. In particular, I had a great deal of support in these tasks: Exam Bank Committee, Invigilators, Marking Committee, Appeals Committee, MCCPM Oral Examiners, FCCPM Examiners, Logistical Support, and I would like to acknowledge the support of the following people (apologies for omissions):

Robert Corns, Sherry Connors, Nancy Barrett, Marc Mackenzie, Terry Riauka, Ian Kay, Jeff Bews, Peter O'Brien, Lise Sullivan, Tatjana Nisic, David Wilkins, Ervin Podgorsak, Horacio Patrocinio, Boyd McCurdy, Tom Farrell, Clement Aresnault, John Grant, Dick Drost, John Rowlands, Michael Hale, John Schreiner, William Parker, Craig Lewis, Andrew Kerr, Vic Peters, Rob Barnett, Francois Deblois, Gord Mausley, Wayne Beckham, Narinder Sidhu, Jake VanDyk, Frank Prato, John Schreiner, Brenda Clark, Katharina Sixel.

2008 Francophone Conference in Medical Physics

L'Association Marocaine de Physique Médicale (AMPM) with the support of the Société Française de Physique Médicale (SFPM) and the Société Belge des Physiciens d'Hôpital (SBPH), is organizing the first Francophone Conference in Medical Physics in 2008.

COMP will certainly be promoting this conference on our website and advertising it to our members. The organizing committee is looking for a Canadian medical physicist to serve on the Scientific Committee.

If this is something that you are interested in or if you would like more information, please contact nancy@medphys.ca
or 613-599-1948.

The American Board of Radiology: Summit on CAMPEP Requirements for Board Certification

Submitted by: Peter Dunscombe
Tom Baker Cancer Centre, Calgary, AB

As most of you probably know, the American Board of Radiology is planning to change, in 2012, the eligibility requirements for certification to include successful completion of a CAMPEP accredited clinical training program (generally understood to mean either a graduate program or a residency). The exact interpretation of the ABR's intention, and the feasibility of implementing it within the stated time frame, is causing concern to many, not least students and education/training program directors. The ABR Summit provided a forum in which an open discussion of key issues surrounding this initiative could be held. About 30 people attended the Summit including the leadership of the ABR, AAPM and CAMPEP. A significant number of program directors were also present. Your correspondent attended as Vice Chair of CAMPEP and a representative of the Canadian Medical Physics community.

As most of you probably know, the American Board of Radiology is planning to change, in 2012, the eligibility requirements for certification to include successful completion of a CAMPEP accredited clinical training program

The Summit started with an overview of the history and background to the ABR's initiative. This was given by Richard Morin, one of three Physics Trustees of the ABR. Over the years, ABR examiners had become increasingly concerned about the level of knowledge of individuals presenting themselves for the certification examination who had not participated in a structured medical physics education program. This observation, together with the fact that the certification process for physicists is one of only two operated by a member society of the American Board of Medical Specialties which does not require completion of an accredited residency program, provoked the current initiative. In 2002, the ABR decided the new eligibility requirement for certification would be implemented in 2012, i.e. with a 10 year lead time.

John Hazle (CAMPEP Chair) described the vision and activities of CAMPEP. As one of the concerns about the ABR initiative is the feasibility of accrediting a sufficient number of programs to meet the 2012 timeline, the guidelines for residency program accreditation were revised in 2006 to provide greater flexibility while not compromising program quality. The paucity of accredited imaging programs (only 2) and complete absence of accredited nuclear medicine programs (an ABR specialty) were topics which generated considerable discussion.

The paucity of accredited imaging programs (only 2) and complete absence of accredited nuclear medicine programs (an ABR specialty) were topics which generated considerable discussion.

Charles Coffey II then presented his perspective as a program director. He pointed out that the AAPM's position on eligibility for certification includes the more stringent requirement of completion of an accredited residency program, not the vaguer "accredited clinical training program", which is the current wording. Dr. Coffey estimated a demand of between 250 – 350 new clinical physicists per year in the US. He also predicted the growth of professional doctorate programs which could ultimately largely replace the present M.Sc. in Medical Physics. A professional doctorate, 4 – 5 years in duration and encompassing graduate level education and clinical training at the residency level, would require students to support themselves and pay university fees each year in such a program.

The final formal talk of the Summit was by Michael Herman, chair of the AAPM's TG133 on Alternate Pathways. He described the contents of the draft report of TG133 which is available to AAPM members on the AAPM website. Dr. Herman emphasized that the real issues are the quality of care for patients and the role that accredited residencies play is assuring the necessary quality.

The discussion which followed the formal presentations suggested a general consensus that the wording of the ABR's intention be changed to reflect the AAPM's position that a CAMPEP approved residency be the requirement for eligibility to sit the ABR certification examination. With that determination, the feasibility of meeting the current timeline of 2012 became the focus of discussion. The main concern here was the unwitting exclusion of students currently in medical physics education and training programs, which may not be CAMPEP accredited, from eligibility for certification. With five years before the new requirement is scheduled to take effect, the student issue was deemed not to be a problem, at least for the therapy track. The final major issue related to the ABR's initiative concerned the date, 2012. What does it actually mean? Application to sit the exam currently has to be made by the September of the year prior. Is 2012 the deadline for the application or for the exam itself?

Report 90 is clear in requiring successful completion of a residency to include the level of knowledge acquired during a CAMPEP approved graduate program. However, what neither Report 90 nor CAMPEP is very clear on is the lengthening of a residency program to ensure that students with no or incomplete medical physics backgrounds do get two full years of clinical training as well as the necessary didactic education

A topic related to the new eligibility requirement is the appropriate education and training of physicists wishing to enter our profession from other branches of physics. This has been a common route in the past and undoubtedly enriched our profession. Report 90 is clear in requiring successful completion of a residency to include the level of knowledge acquired during a CAMPEP approved graduate program. However, what neither Report 90 nor CAMPEP is very clear on is the lengthening of a residency program to ensure that students with no or incomplete medical phys-

(Continued on page 122)

Canadian College of Physicists in Medicine
Examination Schedule 2008

Membership Examination:
Applications due: 4 January 2008
Examination date: Written 15 March 2008
Oral 10/11 May 2008 (Montreal)
Fee: $450.00
Entry decisions announced on or before February 22
(Note: Non-Radiation Oncology specialty orals to be held at the same time as Fellowship orals)

Fellowship Oral Examination:
Applications due: 4 January 2008
Examination date: 1-2 days prior to COMP Meeting in Quebec City (June)
Fee: $300.00
Entry decisions announced on or before February 22 (later for those who do the membership exam in the same year)

Note:

- The application forms, exam study guide, and sample exams are available on the COMP website under the heading "CCPM Certification". Application forms must be the ones currently posted on the COMP website.
- Membership & Fellowship examination application deadlines are set to the same date. This allows the Credentials Committee to review all applications in one time period.
- **It is critical for the success of your application that you respect the deadlines**.

For further information contact the Registrar:

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(Continued from page 121)

ics backgrounds do get two full years of clinical training as well as the necessary didactic education. This is an issue that CAMPEP will need to address.

To wrap up this discussion on the Summit, perhaps an obvious but important point needs to be made. That is that the consensus opinions of the 30 or so attendees are not binding on the ABR. The three trustees present will convey the essence of the meeting to the ABR with the intentions of clarifying the details of the new eligibility requirement by the end of this year, 2007.

So what's all this got to do with the Canadian Medical Physics scene? Quite a lot, actually. Your correspondent is personally convinced that the calibre of physicists entering the profession, and the quality of service offered to patients, will be enhanced with the requirement that they complete an accredited residency program. Physicians, therapists and nurses all have to graduate from accredited programs in order to practise their arts.

If you don't like that argument, try this one. Through the efforts of the CCPM and COMP, and with the support of our colleagues south of the border, Canadian certification is increasingly recognized in the US for the purposes of licensing for example. Can there be any doubt that this privilege will be withdrawn if we do not impose a similar accredited training requirement to that of the ABR to achieve Canadian certification?

The Canadian College of Physicists in Medicine needs to consider, with urgency, imposing an accredited residency requirement for eligibility for certification. The ABR will follow through with its initiative and probably on the proposed timelines.

Through the efforts of the CCPM and COMP, and with the support of our colleagues south of the border, Canadian certification is increasingly recognized in the US for the purposes of licensing for example. Can there be any doubt that this privilege will be withdrawn if we do not impose a similar accredited training requirement to that of the ABR to achieve Canadian certification?

Canadian cancer centre's who have, even occasionally, individuals in training positions, would be advised to review both the revised CAMPEP guidelines for accreditation of residency programs and the draft TG133

CNSC Feedback Forum: Consolidated Radiotherapy Facility Licence

Submitted by: Kavita Murthy
CNSC, Ottawa, Ontario

Cancer treatment centres in Canada operate many types of radiotherapy facilities with different types of Class II prescribed equipment, such as medical accelerators, cobalt teletherapy units, Gamma Knife units and Brachytherapy remote afterloaders. The operation of these facilities is regulated under the Nuclear Safety and Control Act and its associated regulations, chiefly the Class II Nuclear Facilities and Prescribed Equipment Regulations. Within the CNSC, the Class II Nuclear Facilities Licensing Division (Class II division) is responsible for all regulatory activities related to these licences.

The current CNSC practice is to issue a separate licence for each different type of radiotherapy facility with the result that each institution has to maintain multiple CNSC Class II licences. At present, the average number of separate licences held by cancer treatment centres in Canada is four, with some institutions possessing up to seven separate Class II licences. Among other requirements, CNSC regulations stipulate that licensees submit annual compliance reports for each licence they possess and maintain their licensing documents in good order. The institution (licensee) is required to communicate all relevant program or facility related changes to the regulator in a timely manner and when necessary request licence amendments to reflect the changes. Most licences must be renewed on a five year cycle.

For institutions that possess multiple licences, this results in considerable duplication in the documentation which must be submitted and maintained pursuant to licensing. Preparing and processing duplicate documentation multiple times places significant strain on the resources of both licensees and the regulator.

To address this issue, the Class II Nuclear Facilities Licensing Division has established two new licence classifications, or usetypes[1], which will permit such institutions to consolidate their existing Class II Nuclear Facility and Prescribed Equipment operating and servicing licences under a single CNSC licence. These usetypes are:

525 - *Operate medical accelerator and other radiotherapy facilities*, and;
524 - *Operate and Service medical accelerator and other radiotherapy facilities*.

Usetypes and Basic Requirements for Consolidation

Licences issued for the usetypes listed in Table 1 below can be consolidated under one licence, provided that:

a) All of the licensed activities are conducted under the auspices of a single, integrated radiation safety program and;
b) The same organizational management structure and radiation safety officer (RSO) is responsible for overseeing all of the licences to be consolidated and;
c) There is a single radiation safety manual containing a common set of radiation safety policies and procedures that apply to all of the licensed activities.

Any licensee who currently possesses CNSC operating licences for at least two of the categories listed above may apply for consolidation under the appropriate new usetype.

Licensees who have a licence to service class II prescribed equipment (usetype 566) and who wish to incorporate this activity into the consolidated licence should apply for a licence to Operate and Service medical accelerator and other radiotherapy facilities (usetype 524). Licensees who do not perform such servicing should apply for a licence to Operate medical accelerator and other radiotherapy facilities (usetype 525). Consolidated licences will require renewal every 10 years.

Table 1: Usetypes which may be consolidated

522	operate a medical accelerator facility
535	operate an irradiator facility
542	operate a radioactive source teletherapy facility
552	operate a LDR brachytherapy facility
555	operate a HDR brachytherapy facility
558	operate other brachytherapy prescribed equipment
561	operate a radioactive source stereotactic teletherapy facility
566	service class II prescribed equipment

Exemptions

The consolidation described above is only available for operating licences which permit routine operation of Class II Nuclear Facilities and for Class II Prescribed Equipment servicing licences. Class II Nuclear Facilities that are to be constructed, including replacement equipment being installed in existing bunkers, are still subject to the normal process of applying for separate construction and commissioning licences. However, new facilities can be integrated into a consolidated operating licence once commissioning is complete.

Licences for activities regulated under the Nuclear Substance and Radiation Device Regulations, such as manual Brachytherapy (usetype 912) cannot be included under the new consolidated licences at this time. Class II licences held by non-radiotherapy institutions, such as those for research accelerators (usetype 519) and irradiators (usetype 535) at academic/ research institutions, are also not eligible for consolidation at this time.

Application process

The CNSC has put considerable effort into streamlining the application process and Class II division staff will be available for guidance. For detailed information on this process, you can contact the Class II division staff responsible for your institution directly or by emailing me at kavita.murthy@cnsc-ccsn.gc.ca .

1 .The term "Usetype" is used by the CNSC to refer to the different categories of licensed activities it regulates. For example the usetype "522" refers to the licensed activity "operate a medical accelerator facility". You can find the usetype of your license in the "Licensed Activities" section of your license.

Multimodal Contrast Agent for Cancer Detection and Characterization

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Introduction

The rapid clearance profile of conventional CT and MR contrast agents require the use of fast imaging sequences and in many cases repeated administrations. A proven strategy, successfully employed in the pharmaceutical drug delivery field, to prolong the vascular circulation time of small molecular weight agents is to encapsulate them into nano-sized macromolecular colloidal carriers 1. Nano-encapsulation of contrast agents allows for their retention within the endothelial wall of healthy blood vessels, as well as re-routing their clearance pathway from fast renal filtration to a slower uptake process by the reticulo-endothelial system (liver, spleen) 2. Our collaborative group translated the knowledge and experience acquired in the delivery of hydrophilic small drug molecules into the development of a lipid-based colloidal system (liposome) co-encapsulating two small molecular-weight hydrophilic contrast agents, iohoexol and gadoteridol (Figure B, cover page). The resulting macromolecular system is a vascular contrast agent that can be used for combined CT and MR imaging over prolonged timelines. In this way, contrast enhanced imaging can be performed in either or both imaging modalities without the requirement for fast sequences. Furthermore, the co-localized signal enhancement offers potential for improved registration of CT and MR images.

At disease sites with vascular abnormalities, such as tumors with highly permeable vessel networks, the liposome-based agent is no longer retained within the vascular endothelial wall, but it leaks into the interstitial tumor space at a rate that is a function of vessel permeability and interstitial pressure 3-7. Its subsequent interstitial retention occurs due to the lack of a functional lymphatic drainage system 3-7. This enhanced permeation and retention (EPR) effect makes liposomes a valuable tool to detect and characterize sites of increased vascular permeability. Conventional contrast agents have been widely employed in functional CT and dynamic contrast enhanced (DCE) MR for estimation of physiological parameters such as vascular perfusion and permeability. The use of a macromolecular liposome agent may allow for detection of slowly occurring changes, offering opportunity for characterization of longitudinal processes. The true value of this potential image-based biomarker has yet to be explored. However, investigations to date have shown its high stability and low toxicity.

In this report we have compiled some of the key results from two peer-reviewed papers published by our group in Investigative Radiology 8 and Pharmaceutical Research 9, as well as a proceedings of SPIE 10. Specifically, we will focus on the in vitro and in vivo characterization of our CT and MR liposome system, including assessment of size, agent retention, pharmacokinetics, biodistribution, imaging performance, perfusion and permeation in tumors, and acute toxicity.

Results

Physico-Chemical Characterization of Liposome Agent

Liposomes composed of DPPC, cholesterol and PEG2000DSPE in 55:40:5 percent mole ratios were prepared according to a method described in detail elsewhere 8, 9. The size of the liposomes (70-85 nm in diameter) in suspension in filtered water was measured by dynamic light scattering (DLS) using a DynaPro DLS instrument (Protein Solutions, Charlottesville, VA, USA) at 25°C. Liposome morphology was studied by negatively stained transmission electron microscopy (TEM) with a Hitachi 7000 microscope operating at an acceleration voltage of 80 kV (Figure B, cover page). The iodine and gadolinium concentrations in liposomes were determined using a UV assay with detection at a wavelength of 245 nm (Helios g, Spectronic Unicam, MA, USA) and an assay based on inductively coupled plasma atomic emission spectrometry (ICP-AES Optima 3000DV, Perkin Elmer, MA, USA), respectively.

Figure 1 includes the in vitro release profile for both agents under sink conditions in physiological buffer at 4ºC (Figure 1A) and at 37ºC (Figure 1B). As shown, following the 15-day incubation period at 4°C, 8.7 ± 1.5 % and 6.6 ± 4.5 % of the encapsulated iodine and gadolinium were released, respectively, and at 37°C, 9.1 ± 2.5 % and 7.5 ± 1.4 % of the encapsulated iodine and gadolinium were released, respectively. The liposomes were also sized periodically during the incubation period in order to assess their stability. Figure 2 shows that the liposome size remained constant throughout the 15-day period.

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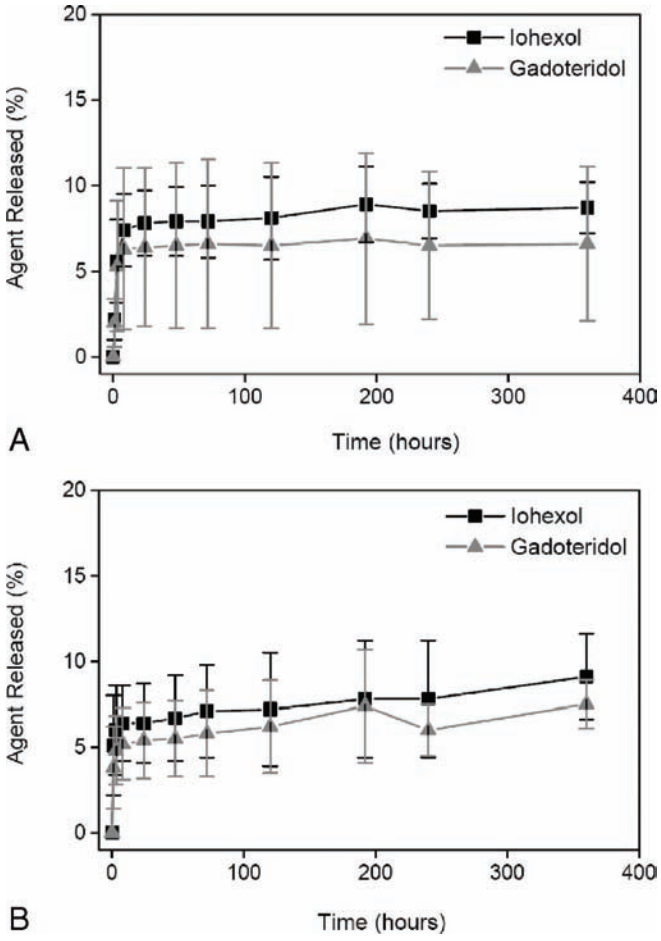


Figure 1: The in vitro release profile for iohexol and gadoteridol from DPPC/cholesterol/DSPE-PEG liposomes dialyzed under sink conditions (250-fold volume excess) against a physiological buffer solution (top) at 4°C (n = 3) and (bottom) at 37°C (n = 4). Data are represented as the mean ± standard deviation. Figure reproduced from Zheng et al. 8.

(Continued from page 124)

Pharmacokinetics and Biodistribution of the Liposome Agent in Animals

The pharmacokinetics and biodistribution studies were performed under protocols approved by the University Health Network Animal Care and Use Committee. Female Balb-C mice (18-23 g) and New Zealand White rabbits were administered slow bolus tail vein (for mice) or ear vein (for rabbits) injections of liposomal contrast agent. At each time point, a terminal blood volume (~ 1 mL) was drawn from a set of 3 mice through cardiac puncture and their organs were harvested for analysis, while an equivalent volume of blood was sampled from the ear vein of the same rabbits over the entire duration of study. Iohexol and gadoteridol were extracted from the plasma and tissue samples and their concentrations were determined using a high performance liquid chromatography instrument (HPLC, PerkinElmer Series 200) and an ICP-AES, respectively [8].

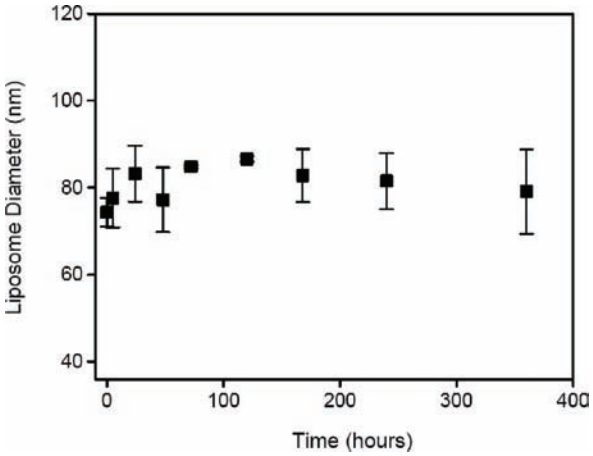
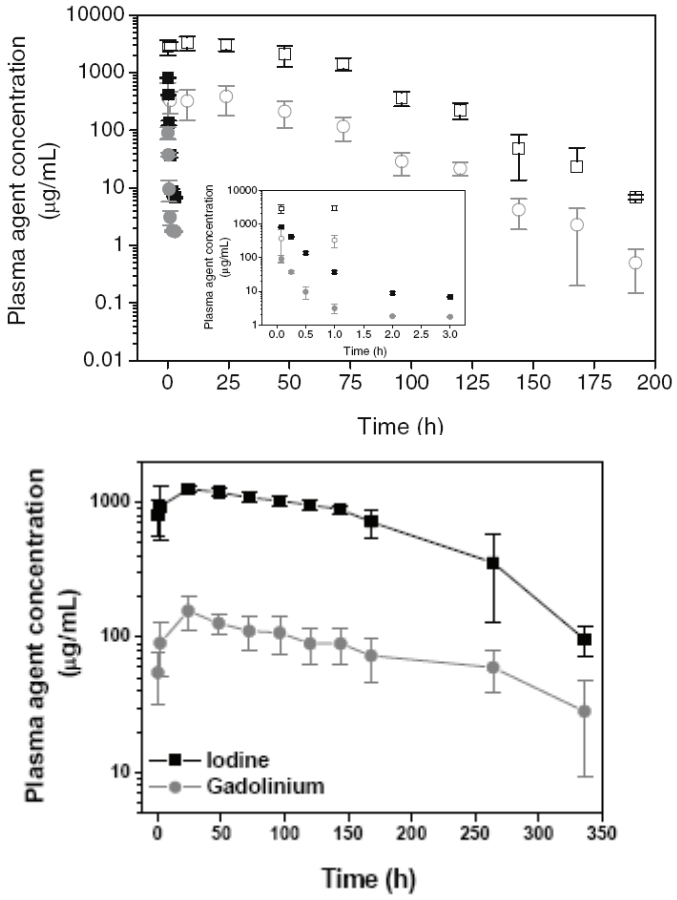


Figure 2: Size of the dual agent-containing liposomes during dialysis under sink conditions (250-fold volume excess) against a physiological buffer solution at 37°C (n = 3). Data are represented as the mean ± standard deviation. Figure reproduced from Zheng et al., 2006 [8].

The data obtained from the pharmacokinetics study was used to determine the main pharmacokinetic parameters for iohexol and gadoteridol when administered as free agents or agents encapsulated within liposomes. For the free agents, a two-compartment model was used to determine the distribution constant (K_d or α) and the elimination constant (K_e or β). The distribution half-life ($t_{1/2\alpha}$) was then calculated using the equation: $t_{1/2\alpha} = \ln(2)/K_d$, while the elimination half-life ($t_{1/2\beta}$) was calculated using the equation: $t_{1/2\beta} = \ln(2)/K_e$. For the liposome encapsulated agents, the K_e value was determined by fitting the plasma concentration versus time curve (each data point represents the mean of three distinct animals) with a one-compartment model. The vascular circulation half-life ($t_{1/2}$) was then calculated using the following equation: $t_{1/2} = \ln(2)/K_e$. The area under the plasma concentration versus time curve (AUC) was calculated using the trapezoid rule. The plasma clearance CL and the volume of distribution V_d were

(Continued on page 128)

Figure 3: Pharmacokinetics of free iohexol (■), free gadoteridol (●), liposomal iohexol (□) and liposomal gadoteridol (○) in healthy female Balb-C mice (n=3) (Bottom) Pharmacokinetics of liposomal iohexol and liposomal gadoteridol in healthy female New Zealand White rabbits (n=2). Plasma was sampled at the indicated time points and analyzed using HPLC for iohexol and ICPAES for gadoteridol. Data are represented as the mean ± standard deviation. Figure reproduced from Zheng et al., 2007 [9, 10].



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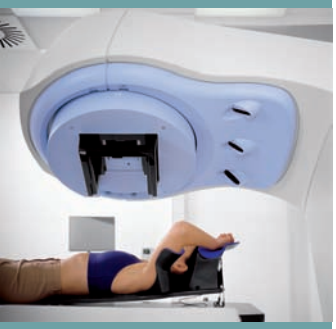

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determined using Equations 1 and 2, respectively, as shown below.

$$CL = \frac{Dose}{AUC \cdot BodyWeight} \quad \text{(Equation 1)}$$

$$V_d = \frac{CL}{K_e} \quad \text{(Equation 2)}$$

Figure 3 includes the 7-day pharmacokinetics profiles (in mice and rabbits) for iohexol and gadoteridol, following i.v. administration in the liposomes, as well as the 3-hour pharmacokinetics profiles for free iohexol and gadoteridol (in mice only). The main pharmacokinetics parameters were calculated as listed in Table 1. In mice, the vascular $t_{1/2}$ for the agents were found to be 18.4 ± 2.4 hours for liposome encapsulated iohexol and 18.1 ± 5.1 hours for liposome encapsulated gadoteridol. The distribution (α phase) half-life for free iohexol was 12.3 ± 0.5 minutes and for free gadoteridol it was 7.6 ± 0.9 minutes, while the elimination (β phase) half-lives were 3.0 ± 0.9 hours for free iohexol and 3.0 ± 1.3 hours for free gadoteridol. The values obtained for the half-lives of the free agents are in agreement with previous publications [11, 12].

	Iohexol	Gadoteridol
K_e	0.0377	0.0383
r^2	0.975	0.980
$t_{1/2}$ (h)	18.4	18.1
AUC (μg*h/mL)	5910000	582000
CL (mL/h/g)	0.00219	0.00206
V_d (mL/g)	0.0580	0.0538

Table 1: Pharmacokinetic parameters for iohexol and gadoteridol when administered in a liposome formulation to healthy female Balb-C mice. Abbreviations: K_e is the elimination constant; r^2 is the coefficient of determination for this fit (every point used for the fit is the mean value obtained from 3 distinct animals); $t_{1/2}$ is the vascular circulation half-life; AUC is the area under the concentration versus time curve in plasma; CL is the total plasma clearance and V_d is the volume of distribution per unit mass. Table reproduced from Zheng et al., 2007 [9].

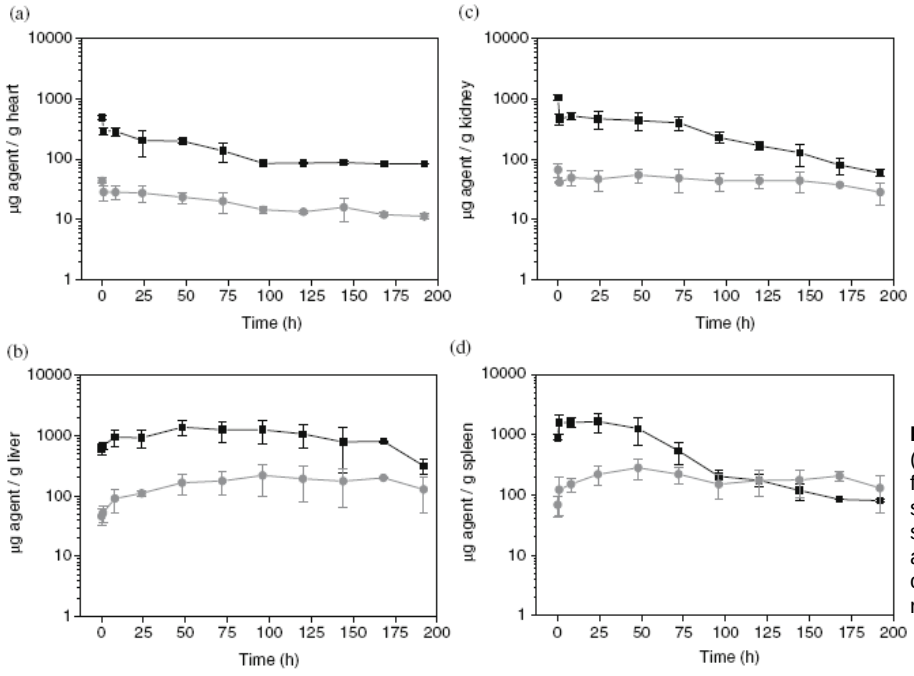

Figure 4: Biodistribution of iohexol (■) and gadoteridol (●) when administered in a liposome formulation to female Balb-C mice. The animals were sacrificed at specific times and a) heart, b) liver, c) kidneys, d) spleen samples were analyzed to determine levels of iohexol and gadoteridol. Each data point represents the mean of three distinct animals ± standard deviation. Figure reproduced from Zheng et al., 2007 [9].

In rabbits, the vascular $t_{1/2}$ for the encapsulated iohexol and gadoteridol were found to be 104.0 hours and 106.6 hours, respectively. The plasma iohexol to gadoteridol ratio over the 11 sampling time points was maintained at 9.2 ± 2.8. The extended and similar circulation half-lives obtained for iohexol and gadoteridol when administered in this liposome formulation suggest that these agents remain co-encapsulated within the formulation *in vivo*.

Figure 4 includes distribution profiles for each agent in the heart, liver, kidney and spleen over a 7-day period in mice. Similar organ distribution and clearance behavior were seen in the heart and liver for iohexol and gadoteridol. While an enhanced elimination of iohexol was observed in the kidney and the spleen compared to gadoteridol. In rabbits, CT imaging-based assessment was used to determine the tissue to blood ratio of the liposome agent (Figure 5). Specifically, regions of interest (ROI) were drawn in CT and the differential signal increase (ΔHU_{rel}) at each pixel within the ROI was calculated for each imaging time using the following equation:

$$\Delta HU_{rel} = \frac{(HU_t - HU_{t=0})}{HU_{t=0}}$$

CT and MR Imaging of Healthy and Tumor-Bearing Animals

Healthy female New Zealand White rabbits (2.8-3.2 kg) were administered a slow bolus injection (0.5 mL/second) of 20 mL of the liposomal contrast agent to their marginal ear vein. Each rabbit received 340 mg/kg of iodine and 20 mg/kg of gadolinium co-encapsulated within the liposomes. Images of the rabbits were acquired pre and post-administration of the liposome formulation in CT (GE Discovery ST, General Electric Medical Systems, Milwaukee, WI, USA) and MR (GE Signa TwinSpeed MR scanner, General Electric Medical Systems, Milwaukee, WI, USA). The rabbits were CT (120 kVp, 200 mA, a voxel size of 0.43 x 0.43 x 0.625 mm^3, and a FOV of 220 x 220 x 400 mm^3) and MR scanned (3D FSPGR sequence with a TR of 9.8 ms, a TE of 4.3 ms, a flip angle of 15°, a voxel size of 0.86 x 0.86 x 1.5 mm^3 over a FOV of 220 x 220 x 228 mm^3, and an image matrix of 256 x 256) at selected times following administration of the liposome formulation.

Figure 6 shows sequential CT and MR images acquired in the same rabbit over a 7-day period. The clear post-contrast visualization of the rabbit heart, liver and spleen, as well as the transient visualization of the kidneys, is in accordance with the presence of the liposomal iohexol and gadoteridol detected in the same organs in mice (Figure 4).

The mean attenuation values in Hounsfield units (HU) in CT and the relative signal intensities (SI) in MR were then measured in the

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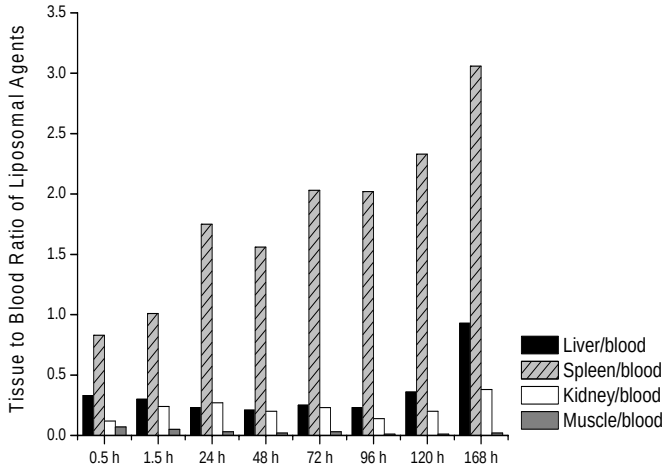

Figure 5 : Biodistribution profiles of agent-encapsulating liposomes in a healthy female New Zealand White rabbit. The tissue to blood liposomal agent ratio was calculated based on the differential signal increase (DHU_{rel}) measured from a region of interest of 0.1 cm^2 in the pre- and post-contrast CT images. Figure reproduced from Zheng et al., 2007 [10].

(Continued from page 128)

aorta with circular regions of interest over a cross sectional area of ~ 9 mm^2 in a single axial image, and correlated to the amount of iodine and gadolinium detected in the 1.5 mL of blood was collected from the ear vein of the same rabbits at the selected time points (Figure7).

Figure A of the cover page (partially reproduced from Zheng et al., 2007 [10]) shows that, administration of the liposome agent two weeks post tumor implantation, in VX2 sarcoma bearing rabbits, results in immediate enhancement of blood vessels, including the extensive vasculature developed around the tumor that is located in the upper left thigh. The extent of tumor vascularization or angiogenesis can be seen by comparison to the non-tumor bearing right thigh of the same animal. At 24 and 48-hours post administration of the formulation, a slow accumulation of the liposomes is seen inside the tumor, likely due to the EPR effect [3-5]. Further studies are underway to correlate the differential signal enhancement rates measured in the distinct tumor regions, which is indicative of the rate of liposome penetration, to the degree of regional vascularization and vessel permeability.

Preliminary Evaluation of Acute Toxicity

Female Balb-C mice were randomly divided into three groups as follows: mice receiving no formulation, mice receiving empty liposomes (700 mg/kg of lipid); mice receiving iohexol (650 mg/kg, equivalent to 300 mg/kg iodine) and gadoteridol (53 mg/kg, equivalent to 15 mg/kg gadolinium) co-encapsulated within liposomes (700 mg/kg lipid). Seven days later blood samples (0.5-1mL) were drawn by cardiac puncture and sent to Vita-Tech (Markham, Ontario, Canada) for haematological and biochemical analysis. The analysis included determination of number of white and red blood cells (WBC and RBC), platelets, and measurement of hematocrit, hemoglobin, serum creatinine, alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST) concentrations. Statistical comparisons of the acute toxicity values were performed using the student t-test [13]. P-values greater than 0.05 were considered to be statistically insignificant.

Figure 8 summarizes the results obtained from the hematological and biochemical analysis of plasma samples obtained one week following administration of both empty liposomes and the liposome formulation of the CT and MR contrast agents. As shown, there were no statistically significant changes (for p=0.05) in the levels of red and white blood cells, hemoglobin, hematocrit, serum creatinine, and various liver enzymes (ALP, ALT and AST), 7 days following administration of the multimodal liposomes in comparison to animals receiving no treatment or those that received the empty liposomes. This study provides a preliminary indication of the lack of toxicity and biocompatibility of this formulation.

Discussion and Future Work

The novelty of the liposome-based contrast agent used in these investigations is its ability to provide simultaneous contrast enhancement in two imaging modalities (CT and MR), its long vascular residency half-life and its preferential accumulation in tumors. The critical size of this liposome agent (~ 80 nm in diameter) enables its confinement within healthy blood vessels, as well as preferential extravasation through leaky abnormal vasculature, such as that found in tumors. Compared to the typical vascular half-life of less than 20 minutes for free iohexol and gadoteridol[9,

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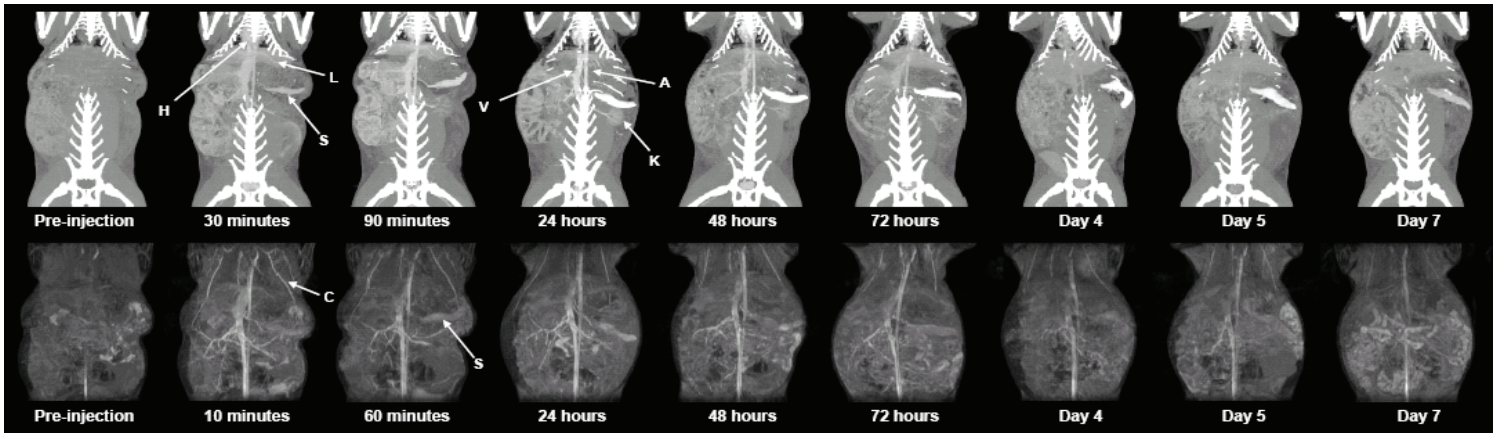

Figure 6: Three-dimensional maximum intensity projection images (anterior view) of a healthy New Zealand White rabbit (3kg) obtained in CT (120 kV, 200mA-top) and MR (3D FSPGR sequence, TR/TE=9.8/4.3-bottom) prior to and following i.v. administration (as indicated) of the liposome formulation of iohexol and gadoteridol. The same window and level were used for pre- and post-injection images. Note the visual contrast changes in the heart (H), aorta (A), vena cava (V), carotid artery (C), kidney (K) and spleen (S). Figure reproduced from Zheng et al., 2007 [9].

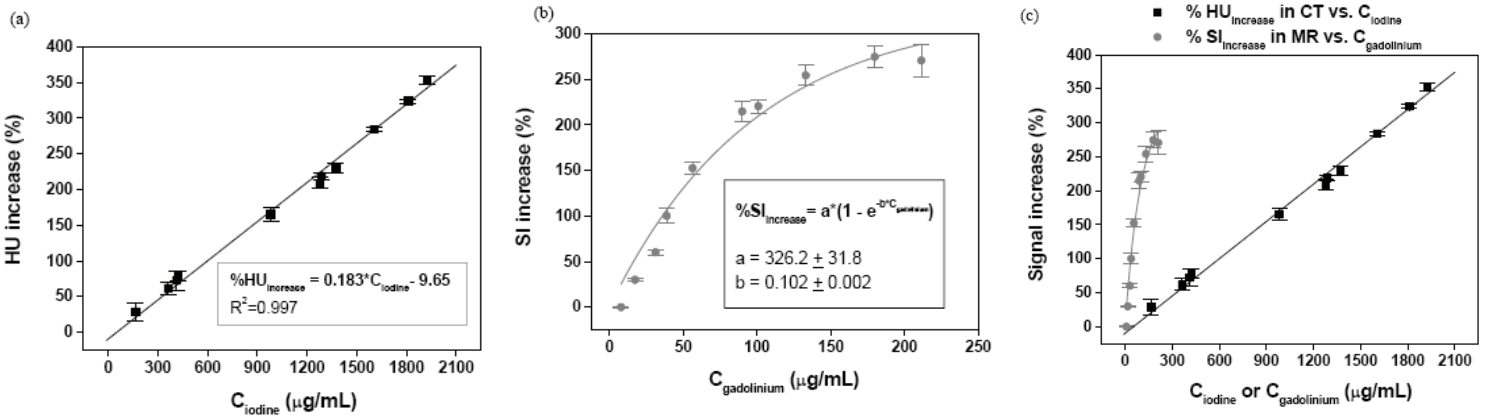

Figure 7: Plots of the relative change in signal intensity pre- and post-administration of the multimodal liposomal agent (left) in CT versus the measured plasma iodine concentration, (middle) in MR versus the measured plasma gadolinium concentration. The $\%HU_{increase}$ in CT was measured using circular regions of interest of 2 mm in diameter in the rabbit aorta and the plasma concentrations of iodine were determined by HPLC (n). The $\%SI_{increase}$ in MR was measured using circular regions of interest of 2 mm in diameter in the rabbit aorta and the plasma concentration of gadolinium was determined by ICP-AES (|). (right) The two plots are combined in a single graph to illustrate the differential response of each modality to different concentrations of the respective contrast agent. Figure reproduced from Zheng et al., 2007 [9].

(Continued from page 129)

[11], the prolonged circulation time (18 h in mice and 105 h in rabbits) achieved though liposomal encapsulation makes this system ideal for 4D (e.g. cardiac and respiratory) and vessel imaging applications, which may involve long or repeated imaging sessions in one or more modalities. The increase in the mutual information [10] following the administration of this agent also demonstrates its potential to improve registration of CT and MR images over extended time frames. Furthermore, the preferential penetration of this agent into the intratumoral space via the leaky angiogenic vessels (Figure A, cover page) allows for its use in detection of disease sites that are associated with abnormal vasculature. The kinetics of the EPR effect may also be monitored longitudinally in CT and MR and used for calculation of physiological parameters, such as perfusion and vessel permeability, to improve characterization of disease state and treatment outcome.

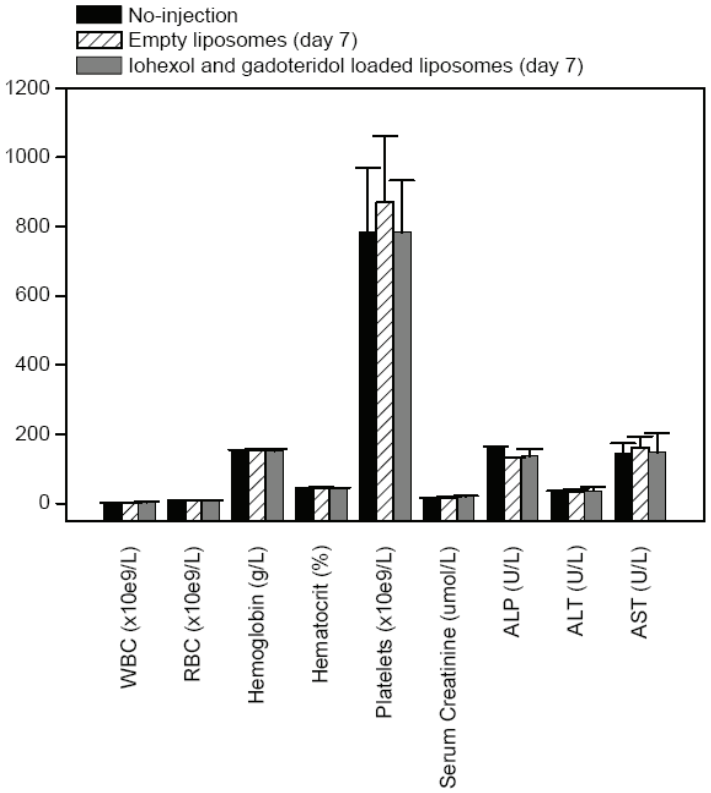

Figure 8: Summary of the hematological and biochemical evaluation of plasma samples obtained from female Balb-C mice (n=3) 7 days following 1) no treatment, 2) administration of empty liposomes, or 3) administration of liposomes containing both iohexol and gadoteridol. Abbreviations: white blood cell (WBC), red blood cell (RBC), alkaline phosphatase (ALP), alanine transaminase (ALT) and aspartate transaminase (AST). Data are represented as the meant standard deviation. For all parameters, the differences between the three groups are found to be statistically insignificant using the student t-test (all p-values were greater than 0.05). Figure reproduced from Zheng et al., 2007 [9].

The flexibility and the stability of liposomes to deliver and retain their load have led to the extension of this carrier platform to support additional imaging modalities, such as SPECT, PET and optical imaging. Current efforts are focused on the development of reliable protocols for quick and effective assembly of the different components in this multimodal imaging kit so that it may be readily tailored to specific applications. In addition, if this platform, which has the ability to be detected over a wide range of spatial resolutions and sensitivities by a variety of imaging techniques, is further modified with the addition of an active targeting moiety, it may become a valuable system to investigate the effectiveness of different molecular targeting strategies (i.e. the degree of specific localization and uptake by the cell population of interest *in vivo* longitudinally). In parallel, our group is also conducting a number of studies to validate the information obtained with this novel agent with results obtained employing current gold standard techniques. The main advantage of our system, compared to other interesting contrast agent developments, is that all of the components employed have been regulatory approved for use in humans. This may accelerate the translation of this technology to the clinical setting.

We hope that this article has broadened the readers' view on contrast agents, from small molecules that transiently perturb the signal generated by a given imaging system, to encompass modular platforms that may be readily tailored and assembled for use in specific applications and directed towards a range of biological targets.

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(For References see page 135)

Construction of Canada's first temporary radiation bunker under way at the Royal Victoria Hospital in Barrie, Ontario

Submitted by: Stuart SC Burnett
Odette Cancer Centre (formerly the Toronto-Sunnybrook Regional Cancer Centre)

Demand for cancer services will only increase as the population grows and the "baby boomers" approach retirement age. The government of Ontario is attempting to meet this demand by funding the expansion of services at existing cancer centres and the construction of new facilities across the province. A visit to the Capital Projects page of the Cancer Care Ontario (CCO) website (http://www.cancercare.on.ca/index.htm) shows that some of these facilities are already operational and ramping up their capacity. Others are under construction or are still in the planning stages.

In 2005, residents of Simcoe County and the District of Muskoka in Central Ontario welcomed the news that the Simcoe-Muskoka Regional Cancer Centre (SMRCC) is to be built at the Royal Victoria Hospital (RVH) in Barrie, Ontario. Construction is due to begin in Fall of 2008 with completion in early 2011. Welcome news, indeed ! Currently, radiotherapy patients from the Barrie area face a 100 km drive to Toronto down highway 400, often in difficult conditions. For those who can travel, it means a long commute for several weeks of treatment. For those who can find accommodation in Toronto, it can mean separation from the support of family and friends. The new centre will remove this added burden by bringing cancer treatments closer to home.

But what of those patients who are diagnosed before the new centre opens ? A US company, Rad Technology Systems, has marketed a remarkably simple solution that accelerates access to radiotherapy in communities where it is lacking: a temporary radiation bunker based on a prefabricated modular design (http://www.rad-technology.com). The modules resemble shipping containers both in shape and size, and are stacked, like giant toy bricks, to form the bunker. Shielding is provided by steel plates surrounded by a proprietary granular fill, and by borated polyethylene[1]. The facility houses a single linac, and comes with a console area, exam rooms, office space, etc. These auxiliary structures are also modular and fit onto the side of the bunker. The technology has been deployed in the US and UK, but the Barrie site is scheduled to be the first in Canada, with a second to follow in Ottawa a few months later. Both sites will house the Elekta Synergy platform.

The RVH has partnered with CCO and the Odette Cancer Centre (OCC) at the Sunnybrook Health Sciences Centre in Toronto to develop a radiation program around the temporary facility. Radiation oncologists, radiation therapists, dosimetrists and medical physicists from the OCC will collaborate with staff at the RVH to plan and provide radiation treatment services. The accelerated timeline (funding for the RadTech bunker announced in May, construction started in late August, the linac due in October, and treatments to begin around the New Year) promises to be a godsend for hundreds of cancer patients from the Barrie area. Three years from now, once the SMRCC is completed, the bunker will be dismantled, the linac moved to its permanent home, and the bunker made available for use at a different location.

1. "Shielding evaluation and acceptance testing of a prefabricated, modular, temporary radiation therapy treatment facility", G.A.Ezzell, *Journal of Applied Clinical Medical Physics*, **5** (4), 120-125, (2004).

Construction site for the temporary radiation bunker at the Royal Victoria Hospital, Barrie, Ontario, taken on August 30, 2007. The concrete pad, which will support the linac, and the outline of the auxiliary structures are clearly visible (photo courtesy of Garth Matheson, VP Regional Cancer & Clinical Services at RVH).

Toronto ICCR Conference

(+ physic break-dance fever 2007)

Submitted by: Parminder S Basran
Odette Cancer Centre

Toronto hosted the International Conference on the use of Computers in Radiotherapy (ICCR) which is held once every three years. I always expect this to be a good conference since many important advances in radiation therapy physics can be traced from seminal papers presented at an ICCR conference. This years scientific program did not disappoint in providing attendees what we should be expecting in the next several years.

I have to confess that I live in Toronto, so I am clearly biased and cannot provide a visitors perspective on the activities outside of the conference. To help minimize the bias, I pretended to be a tourist when taking the subway down to the conference hotel. I prominently displayed my name tag, carried my new conference bag and was nice to strangers on the subway.

Printouts for the scientific proceedings were heavy. *Very* heavy. So heavy that the strap on my new conference bag snapped (really!). With my abbreviated program in hand, I prepared to dive into the scientific sessions. The sessions started with some excellent talks from Drs Jack Cunningham, Benedick Fraass, and Jerry Battista. The reviewer's choice sessions followed immediately afterwards, which were the top five abstracts submitted to the conference (plug for Canadian Karl Otto from Vancouver for his session on Single Arc IMRT treatments!). There were many talks on cone-beam imaging, image registration, motion modeling, image guidance and adaptive strategies. Many of the presentations had less emphasis on the word "computer" and more emphasis on "radiation". There were a number of innovative talks on new technologies, such as proton beams, functional imaging systems, and hybrid MRI/ proton treatment facilities. Perhaps we are in a cycle where there are more technological advances than innovations in computers. But as in any conference, I was inspired as much as I was overloaded with fresh ideas and questions.

As always, it is always nice to see old colleagues and make friends ones at conferences. It was particularly nice to show them how colorful and vibrant Toronto is. But since the writer is biased, I invite you to check this out for yourself at the COMP/CARO meeting.

The 'night out' was a beach party at Toronto Island. The ferry ride on Lake Ontario provided many beautiful vistas of Toronto's skyline and the waterfront. Once across the lake, the signs pointed us to the restaurant/bar adjacent to the ferry dock (perhaps there was some foresight to keep the drinks within stumbling distance from the ferry!). While the weather was a bit cold and damp, it did not dissuade soccer and Frisbee enthusiasts from partaking in some exercise. Inside the restaurant, the band played a mish-mash of R&B/funk/pop/jazz that generally resulted in a lot of rump-shaking, some very bad break-dancing, and the a few strange bouts of hand-stands on the dance floor. Fortunately, there were ICCR towels that could be used to fan the dance-fever (or blind-fold us from the MC Hammer impersonations). Amazing what a few drink-tickets and some good music can do a physicist.

The scientific conference proceeded the next day bright and early, and you could tell that there were a few sore bodies in the audience. After winding up the scientific sessions, it was time to pass the baton to another city to host the next ICCR. The next conference is scheduled for 2010 and the Netherlands Cancer Institute kindly accepted as the host of the event. It should prove an excellent venue for science and fun! See you there in 2010!

From the Editor:

COMP Archives to Wikipedia to Bobo the Ninja

I cannot believe it has been a year since I first took over the reigns as Editor for our Newsletter. So far, it has been a very interesting and rewarding experience. While it is a bit time-consuming, it is getting easier after every edition and I am starting to feel like a more confident and *competent* as Editor. Your continuing contributions to the Newsletter make the job much easier: note that the alternative is reading more words from despotic editors. So, please! Keep those articles coming. If you know someone in your lab who has some interesting research, share it!

On that note, the 'In-Brief' section has been non-existent while I have been Editor. To remind our readers, the 'In-Brief' section are tid-bits of information that may be of interest to the broader medical physics community. So again, even if it is a 'one-liner', please consider contributing to our Newsletter.

I recently contacted Dr Peter Munro, whose name some of you might recognize: he was one of our past Editors (and a very *competent* one, being largely responsible for the look of the Newsletter you see today). He was kind enough to parcel out a package of old editions of the COMP/CCPM Newsletter dating as far back as 1981. The package sits by my desk and proves to be fascinating and a welcome addition to our COMP archives. I was pleased to see that the first "Editor" of a formal Medical Physics Newsletter was Ms Karen Breitman, then from Manitoba, now in Calgary (alma matter of the current Editor). Back then, the Newsletter was a publication of the Division of Medical and Biological Physics in the Canadian Association of Physicists. In one of the first few articles was a discussion paper from Dr John Aldrich entitled: *Medical Physics in Canada: Is it time for a Canadian Association of Physicists in Medicine?* There he writes about the newly formed CCPM:

(Continued on page 134)

Opening of the R.S. McLaughlin Durham Regional Cancer Centre

Submitted by: Darcy Mason
RS McLaughlin Durham Regional Cancer Centre

The R.S. McLaughlin Durham Regional Cancer Centre (DRCC for short) is the newest addition to the radiotherapy-capable centres in the greater Toronto area. The DRCC is located just north of downtown Oshawa, about 50 km east of Toronto, and is part of the Lakeridge Health Oshawa hospital. It is named after the late R. Sam McLaughlin, local philanthropist and founder of the McLaughlin Motor Car Company, the precursor to General Motors of Canada.

The DRCC has actually existed as a funded program for many years, with radiation treatments delivered in the evenings at Sunnybrook in Toronto. However, it is only in 2006 that the program started to approach the long-awaited goal of having its own building. Chief physicist Dr. Katharina Sixel began working (along with RT manager Sharan Manship) in February 2006; admin support Su Horn joined in May 2006. Other physicists (Darcy Mason, Daryl Scora, and Cathy Neath) joined from mid-September through late October. I.T. specialist Ehab Fanous also started in September, with a dual-reporting relationship to I.T. and Physics. Our service engineer, Bogdan Koscik, started in Dec. 2006.

Through the fall we researched and purchased equipment and software to lay down the infrastructure for the work ahead. Katharina and Daryl traveled to Germany to participate in the Velocity program, in which linac data is measured at the factory before delivery. Major equipment began arriving in Dec 2006 (see text box for equipment details). First the CT scanner (early Dec.), then three linacs arrived just in time for Christmas; they were installed and accepted by the end of January. Dosimetrists and therapists arrived through the spring of 2007. Due to the inevitable construction delays, we had limited access to the building until January, and did not officially move in until the end of April. Hard hats and safety boots were mandatory for what seemed like an endless stretch of time. Prior to gaining occupancy, we had (happily) coexisted for many months in a small space in the hospital.

After the linacs were delivered, the pace of developments accelerated. From January to May, we commissioned the linacs and the treatment planning system, and developed treatment policies and techniques. The first treatment day was on May 7 and within a month, we reached our treatment capacity. We recently started running extended hours (10 hour day) on one treatment unit, with the others to follow when new therapist staff are in place.

We are quite proud of the amount we accomplished in a relatively short time. We worked with the major software vendors to create a fully paperless/filmless electronic record, with all systems linked into our central 6 TB SAN storage. We had both IMRT (prostate) and IGRT (MV cone-beam of implanted gold seeds) available on opening. DRCC's philosophy is that, although as a smaller centre (compared with our Toronto neighbours) we may not treat all sites, we will offer state of the art for what we do.

DRCC Quick Facts:

- 90000 square feet
- Approx 1800 new patients/year
- 7 bunkers, 3 currently filled (Siemens Oncor linacs with flat panel/MV cone-beam)
- 2 sim suites, one filled (Siemens Somatom)
- CMS treatment planning software
- Lantis electronic record
- HDR planned for spring 2008

We expect the fast pace to continue for many years. Plans are already starting for approval of a fourth linac, which we hope could be in place by summer of 2008. We plan to use the seventh bunker, an unfinished concrete shell, as a "swing bunker" to help with the clinical load during upgrades or replacements. An HDR program is being planned to start in spring 2008. With all the increases in equipment and services, keep your eyes out for new job postings!

The physicists with the first linac being delivered through the atrium. From left, Darcy Mason, Cathy Neath, Katharina Sixel, and Daryl Scora.

The R.S. McLaughin Durham Regional Cancer Centre.

The COMP Gold Medal

The COMP Gold Medal will be awarded to a member of COMP (or retired ex-member) who has made a significant contribution to the field of medical physics in Canada. A significant contribution will be defined as one or more of the following:

1. A body of work which has added to the knowledge base of medical physics in such a way as to fundamentally alter the practice of medical physics.
2. Leadership positions in medical physics organizations which have led to improvements in the status and public image of medical physicists in Canada.
3. Significant influence on the professional development of the careers of medical physicists

in Canada through educational activities or mentorship The Gold Medal is the highest award given by the Canadian Organization of Medical Physicists and will be given to currently active or retired individuals to recognize an outstanding career as a medical physicist who has worked mainly in Canada. It will be awarded as appropriate candidates are selected but it will not generally be given more than once per year.

Nominations for the 2008 medal are hereby solicited. Nominations are due by Dec 15 each year and must be made by a member of COMP. Nominations must include:

- the nominator's letter summarizing the contributions of the candidate in one or more of the areas listed above;
- the candidate's CV;
- the candidate's publication list (excluding abstracts) which highlights the candidates most significant 10 papers;
- additional 1 to 2 page letters supporting the nomination from three or more members of COMP.

The applications will be made electronically to Nancy Barrett at the COMP office (preferably in pdf format, nancy@medphys.ca) and authorship of the submission e-mail will be verified by the COMP Office.

A committee of COMP members appointed by the COMP executive will consider nominations and recommend award winners to the COMP executive by Feb 15. The COMP executive makes the final decision and the awardee will be notified by March 15 to give time to arrange a public address at the COMP annual meeting in Quebec City.

Candidates selected for the medal will be invited to attend the annual COMP meeting where the award will be presented by the COMP chair. Travel expenses will be paid for the medal winner. The medal winner may be asked to give a 30 min scientific presentation at the COMP meeting in addition to a short acceptance speech when the medal is presented.

> *"(CCPM) was formed a few years ago to encourage the training of Medical Physicists and to establish professional levels of competence. Although (the CCPM) has been met with some skepticism in some parts it is clear that this type of fellowship is being introduced in many countries including the United States, Britain and Australia."*

It is interesting to see to topic of 'competency' in Medical Physics repeat itself even today (see the CCPM presidents message and Dr Dunscombe's report from the ABR Meeting).

On the lighter side of competency, I was interested in what type of reliable information might be available regarding Medical Physics on the web. Out of curiosity, I typed in the words 'Medical Physics' in Wikipedia. After following a few links, I came across web pages that had the words 'EDIT' alongside each of the written texts. I clicked it and started to feel like a blind, thumbless plumber stumbling towards a CT with the gantry covers off (incompetent). After stopping myself from inflicting damage, I pondered: who are the contributors of these rather finely crafted words?

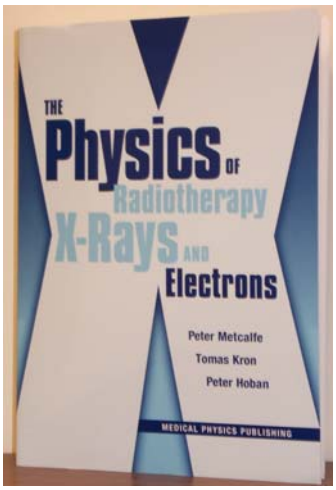
After seeing some rather anonymous contributors, I noticed that characters by the names of 'kungfuadam' and 'Bobo the Ninja' appeared to be editing some of the pages. It turns out that Bobo is a self-proclaimed expert in chemistry who attends Rock Bridge

(Continued on page 136)

Book Review:

The Physics of Radiotherapy X-Rays and Electrons

Peter Metcalfe, Tomas Kron, Peter Hoban



905 pages.
Medical Physics Publishing.
Price $140 USD
(hardcover
ISBN: 978-1-930524-35-4)
or
$120 USD
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ISBN:978-1-930524-36-1).

This updated successor to ***The Physics of Radiotherapy X-Rays from Linear Accelerators*** (1997) is almost double in pages from the previous book and includes a significant amount of new material on state of the art tools and modalities in radiotherapy (EPID, OBI, IMRT, IGRT and Tomotherapy) as well as updated chapters on electrons in radiotherapy, beam modeling and radiobiological modeling. Selected questions and answers from ***The Q book, the Physics of Radiotherapy X-Rays: Problems and Solutions*** have been refreshed and integrated into this book, combining the best of a reference textbook with inclusion of exam questions for the physics teacher or student.

Many new diagrams and images complement the text, with full colour plates in the center of the book that show advanced tools and complex isodose plans for the new modalities. As a teacher of physics, I liked this book very much because it conveniently consolidates reference material from many recent sources to explain a topic. An example is the new section on electron beam properties which has extensive diagrams such as Monte Carlo calculated particle tracks, to clarify the topic and make it more visual for the student.

The old dosimetry chapter has been split into two chapters, one focusing on dosimeters and the other on the Calibration of Megavoltage beams. The later is very useful to the clinical physicist, with details of the calibration procedures and a comparison of the multiple international dosimetry protocols available. The updated dosimetry chapter includes a thorough treatment of the traditional detectors used in oncology today, but also has details on the rarer diamond detectors, radiochromic film and gel dosimetry tools, to name but a few.

The new emerging technologies chapter on Stereotactic Radiosurgery, IMRT and Tomotherapy is an excellent introduction to these topics. It gives the reader an easy way to compare the 3 modalities for pros and cons of each specialty. Ample references at the end of the chapter will lead the reader on to any details missing.

The beam modeling section has been updated to include more details on electron pencil beams. The authors make an effort to comment on the consistency of the various models with phantom measurements as they take you from early models to collapsed cone.

The clinical physicist will also find the new chapters on QA in Radiotherapy, Radiation Protection and Room shielding and Patient Immobilization and Image Guidance to be very useful. Although these topics are presented in the literature elsewhere, they are treated comprehensively in one section and include the references for further study. . There is more emphasis on specific clinical procedures not usually found in journal articles.

The book is an excellent resource for the novice professional for clinical practice and as a updated review for the experienced professional. I would highly recommend it as a valuable addition to the library of all practicing clinical physicists, teachers and students of radiation oncology physics and would recommend it as required reading for CCPM candidates.

(Continued from page 130)

Email: jinzi.zheng@rmp.uhn.on.ca

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The 21st L H Gray Conference

The Radiobiology – Radiation Protection Interface

Radiobiology, epidemiology, and validity of radiation risk estimates in modern radiation practice

4 – 6 June 2008

The Royal College of Physicians, Queen Street, Edinburgh, Scotland

A major international meeting which will bring together experts in radiobiology, epidemiology, and risk assessment, and scientists and clinicians involved in diagnostic and therapeutic radiation exposure

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Radiobiology

- Radiation-induced DNA damage recognition and response
- Non-targeted effects of radiation risk
- Adaptive response in radiation risk

Epidemiological studies

- Exposure to high natural background radiation: what can it teach us about radiation risk?
- Non-cancer effects in Japanese bomb survivors
- Chernobyl: what have we learnt from it?
- Radiation in the workplace

Uncertainties in risk estimation

- Bio-kinetic modelling and risk
- How confident are we that we can calculate radiation risk?

Issues in radiation practice

- Issues in diagnostic medical exposures
- Mammography – oncogenicity at low doses
- Implications of the bystander effect for radiotherapy
- IMRT, protons and secondary cancers
- Radiation terrorism: what have we learnt from polonium-210
- Radiation terrorism: should the radiobiology community be doing something?
- Is there a place for quantitative risk assessment?

Keynote lecturer: Eric Hall. **Other confirmed speakers:** Elizabeth Cardis, Norman Coleman, Alex Elliott, Nick Gent, Dudley Goodhead, John Harrison, Geoff Heyes, Jolyon Hendry, Steve Jackson, Bleddyn Jones, Ron Mitchel, Bill Morgan, Alastair Munro, and Richard Wakeford

Meeting organizers: Colin Martin, David Sutton, Catharine West, and Eric Wright (Chair) for the **L H Gray Memorial Trust** and the **Society for Radiological Protection**

Further details: **http://www.srp-uk.org/events/lhgray2008**
or e-mail colin.martin@northglasgow.scot.nhs.uk

2015 International Federation for Medical and Biological Engineering's World Congress

Background

- COMP has been approached by the City of Vancouver to consider participating in a bid to host the 2015 IFMBE World Congress, a triennial event that attracts over 3000 attendees
- This congress has not been to Canada since 1976 when it was in Ottawa.
- The IFMBE requires that applications to host the World Congress must be submitted jointly by the national IFMBE and IOMP affiliates (in this case CMBES and COMP) indicating their mutual commitment in the planning, preparation and financial management of the World Congress.
- Bids are due in 2009

Why bid?

- International recognition for COMP
- Providing Canadian medical physicists with an opportunity to attend an international event at a lower cost
- Networking opportunities
- Information exchange and cooperation
- Potential financial rewards (other organizations have used profits for special projects, scholarships, exchanges etc)

Why Not Bid?

- Time required to prepare bid and lobby decision-makers
- May not be successful
- Potential financial risks of hosting an international congress

The next step is determining if there is sufficient interest and the resources within the COMP membership for a bid team and/or organizing committee.

Please contact me at nancy@medphys.ca or 613-599-1948 if you would be interested in getting involved or if you would like more information.

(Continued from page 134)

High School in Missouri. I don't know what kind of journals you are reading, but I haven't cited or read many works from Bobo yet. (Try this at home! Type "Radiation Therapy" in Wikipedia, scroll down to "Mechanism of action", select 'EDIT' on the right, and then "edit history" in the first paragraph. Scroll through the various pages of edits and you'll find Bobo).

Some interesting facts about Wikipedia:

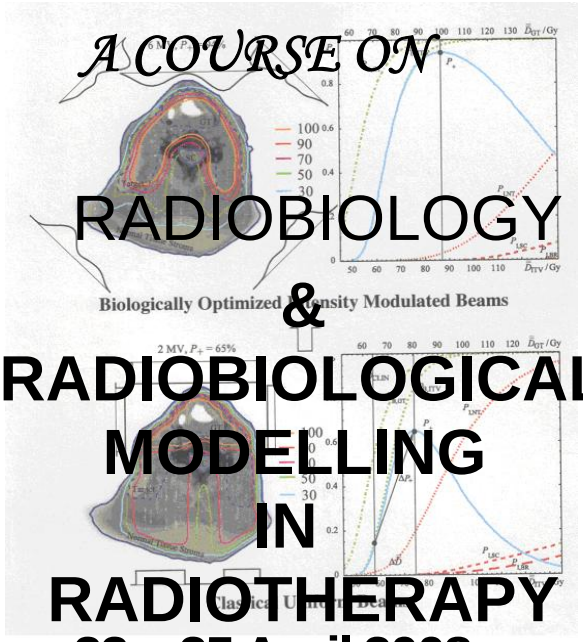
- Wikipedia is a free internet encyclopedia that *anyone* can edit
- There is a entry of 'Wikipedia' on Wikipedia
- According to a peer reviewed study published in *Nature*, Wikipedia is as reliable as an encyclopedia in the accuracy of information provided (something the traveling Britannica salesman failed to mention).

To me, Wikipedia is a shining example of how good -and bad- things can get when you mix science and everyday life. Theoretically, if you wait long enough, any falsehoods, or 'graffiti', would be replaced with a majority consensus opinion on the "correct" description. Interesting concept. I just hope those volunteers adding to the website are *competent*. Sounds like digital Darwinism. Stephen Colbert, a comedian/political satirist calls it "bringing democracy to knowledge", which I found particularly funny, and scary.

I suppose I should get back to work. Now, how exactly should I be calibrating that linear accelerator? Hmmmmm….so much for competency! See you all at COMP/CARO!

Parminder S. Basran

Information also at: http://www.wirral.nhs.uk/uploads/documents/CCORBLGYCOURSEFLYERApril08.pdf



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Professor Roger Dale, Imperial College, London, UK
Dr. Charles Deehan, Guys and St. Thomas' NHS Trust, London, UK
Professor Trevor McMillan, Lancaster Univ., UK
Dr. Hooshang Nikjoo, NASA, Houston
Dr. Marco Schwarz, Agenzia Provinciale per la Protonterapia, Trento, Italy
Dr. Catharine West, Academic dept. of Radiation Oncology, Christie Hospital, Manchester
Dr. Ellen Yorke. MSKCC, New York
Dr. John Fenwick, CCO .
Dr. Andrzej Kacperek, CCO
Dr. Geoff Lawrence,
Dr. Philip Mayles, CCO
Professor Alan Nahum,
Dr. Isabel Syndikus, CCO

For registration details Please contact:
Sue Nixon, Radiobiology Course Secretary, Physics Department, Clatterbridge Centre for Oncology, Clatterbridge Road, Bebington, Wirral CH63 4JY, UK
Tel/Fax: +44 (0)151 482 7860;
Email: Sue.Nixon@ccotrust.nhs.uk

The course provides the background to understand both the basis of radiation treatment for cancer and the use of radiobiological models in the evaluation and optimisation of radiotherapy treatment plans.

It is suitable for anyone involved in Radiotherapy: Radiation Oncologists (especially those in training for (UK) FRCR part I), Physicists, Therapy Radiographers, Researchers and University Teachers.

Days 1 and 2 will cover fundamentals – clonogenic assays, cellular response to radiation, the effect of doserate, radiation quality (LET), cell-cycle effects, the influence of oxygen, the linear-quadratic (LQ) formula and its limitations, the 5 Rs of Radiotherapy, the principles of fractionation and specific considerations in LDR and HDR brachytherapy.

Days 3 and 4 are dedicated to the basis and use of radiobiological models (TCP, NTCP, EUD) in both the evaluation and optimisation of radiotherapy treatment plans.

This is the first-ever course giving extensive coverage, including hands-on practice, to these modeling tools, which are beginning to be available in commercial treatment planning systems.

The teaching faculty is composed of Radiobiologists, Radiation Physicists and Radiation Oncologists who are internationally known for their research and are experienced at teaching various aspects of Radiobiology and its application to Radiotherapy.

Students may bring with them, in poster format, presentations of Radiobiological Modeling work going on in their own departments; these will be displayed for the duration of the course.

VENUE

All the lectures and practical sessions will take place at The CHESTER GROSVENOR AND SPA, Eastgate, Chester CH1 1LT, Cheshire, UK (www.**chestergrosvenor**.com). The CHESTER GROSVENOR is in the heart of the old Roman city of Chester.
Chester is some 25 miles from Liverpool, and within reach of both Manchester and Liverpool airports.

By arrangement, it will be possible to view the spacious and modern Radiotherapy facilities at CCO, which include the UK's only proton-therapy facility as well as *cone-beam* and 4D CT.

Course Organiser: Professor Alan E. Nahum, Physics dept., Clatterbridge Centre for Oncology, to whom enquiries should be addressed (email: alan.nahum@ccotrust.nhs.uk; tel: +44 (0)151 334 1155 extn. 4169)

Alberta Cancer Board

SECOND ANNOUNCEMENT

Workshop

On

Modeling Tumour response to irradiation

May 28-May 31, 2008

Cross Cancer Institute, Edmonton, AB, Canada

Topics

Poisson and non-Poisson TCP models.
Individual- versus Population-based TCP models.
The radio-resistant clonogens, do they really determine the TCP?
Accounting for hypoxia in TCP models.
Implementing TCP models in Radiotherapy TP systems.
Predictive assays.
Tumour growth.
Constructing experiments for TCP-model testing.

Organisers:
Alan Nahum (UK)
Gino Fallone (Canada)
Pavel Stavrev (Canada)

Inquiries:
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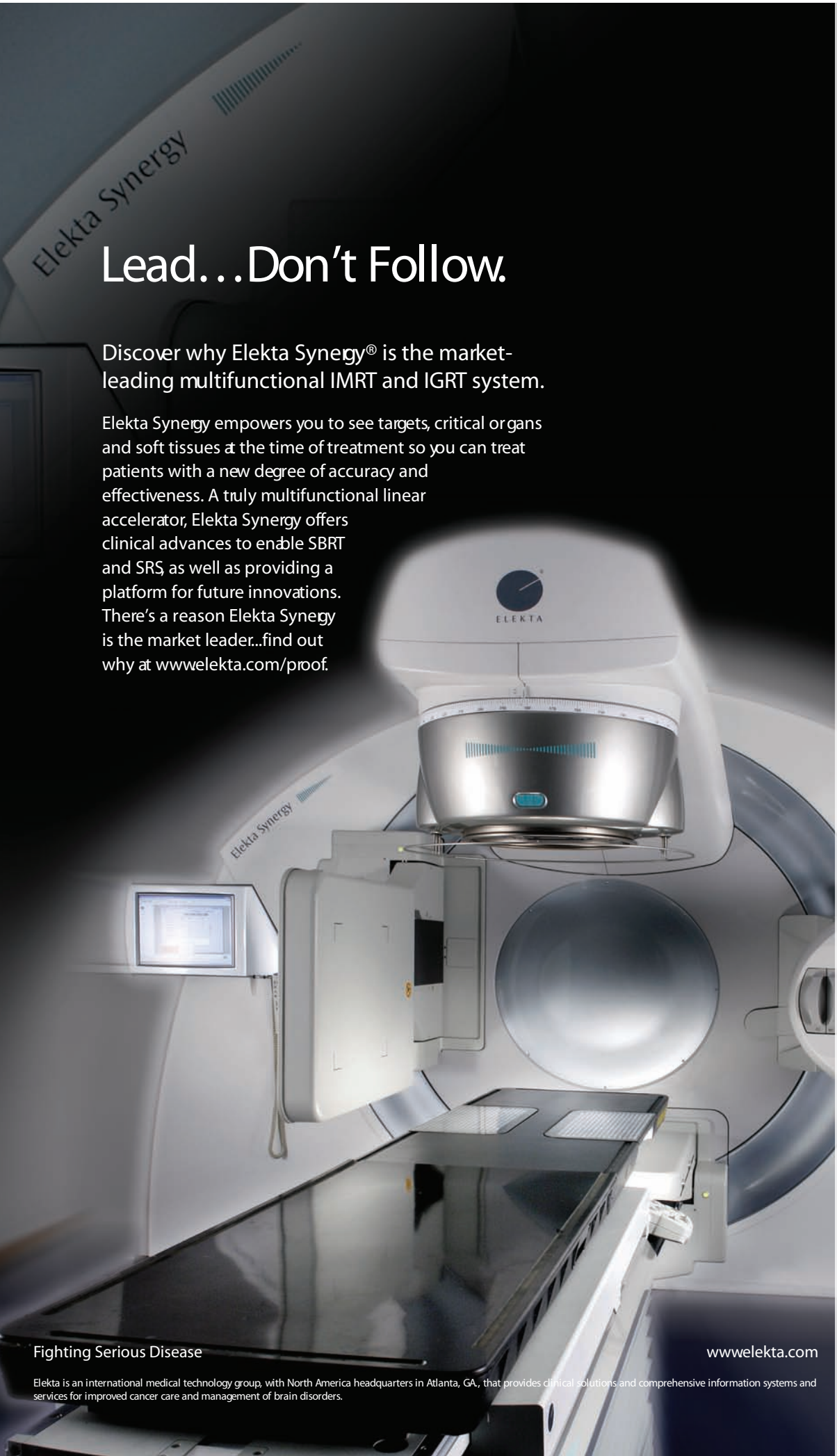

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