Bulletin

Canadian Radiation Protection Association
Association canadienne de radioprotection

Vol 34 No 3
Supplement

Supplemental Report from Conference 2013

by Nick Sion

The *CRPA Bulletin* is published quarterly and is distributed to all members of the association.

Le *Bulletin ACRP* est publié trimestriellement et distribué à tous les membres de l'association.

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2013 Annual CRPA Conference

A Summary of Presentations and Workshops

By Nicholas Sion

CRPA's 2013 conference was held in Sherbrooke, Quebec, on May 26–30. Following is a first-hand account from member Nick Sion of the sessions he attended.

CRPA's 2013 conference focused on lowering radiation dose in medical applications, including from cell phones and from radon, with a review of preclinical molecular imaging in cancer treatment therapy using positron emission tomography (PET) and single-photon emission computed tomography (SPECT) scanners and the generation of ^{99m}Tc by cyclotrons.

The keynote speaker, Roger Lecomte,[1] elaborated on the rationale of using *in vivo* preclinical molecular imaging on small animals and the use of SPECT and PET scanners supplemented by X-ray computed tomography (CT) scanners. These advanced machines have resulted in high doses to staff and to animals used in experiments. Rats and mice, for example, host large numbers of human diseases, and these can be studied under controlled non-invasive conditions prior to clinical therapy. The LD50/30[2] for a mouse is ~ 5 to 7.5 Gy but the recovery from residual radiation damage follows an exponential time course. Repeated sub-lethal doses reduce the survival time (in a mouse approximately −7%/Gy). In humans, a dose of <1 Gy induces some blood cell destruction and releases free radicals. Doses of 5 to 200 cGy induce cell resistance to subsequent therapeutic radiation, that is, adaptive response. However, doses of 1 to 20 cGy are reported to induce therapeutic effects in tumour cells.

Molecular targets and biomarkers are identified for drug-binding sites and gene-therapy assessments as well as for dose regimen and for drug toxicity. Multimodality imaging is the preferred method since PET/SPECT provide information on metabolism, molecular targets, receptors, and on drug-binding sites, whereas CT or magnetic resonance imaging (MRI) are for tissue morphology, tumour volume, etc. The methodology of preclinical in vivo imaging has the advantages of being non-invasive, longitudinal (using the same animal as its own control), and reduces the radiation exposure by the more rational use of radiation flux.

The International Commission on Radiological Protection (ICRP)[3] has publications on radiation protection in medicine, based on risk-benefit to the patient, optimized on the ALARA (as low as reasonably achievable) principle with doses commensurate with the medical purpose of the dose to the patient. Cataract induction to the lens of the eye is at ~ 5Gy, 95% CI (confidence interval) where opacities begin to show. For circulatory diseases (cardiovascular and cerebrovascular) the threshold is at ~ 0.5 Gy with considerable uncertainty if the dose response is below 0.5 Gy. The time to develop cardiovascular and cerebrovascular fatality is >10 years.

The highest sources of artificial exposure are shown in Table 1. The International Radiation Protection Association (IRPA) is the international counterpart of CRPA with some 18,000 members from 61 countries and 48 associated societies. IRPA fosters an understanding of safety culture and engenders communication between the member societies.

Table 1: Medical exposures for circulatory diseases.

Source	Global Average Dose
mSv/year	
Medical diagnosis	0.6 and growing
Occupational	0.005
Nuclear testing	0.005
Chernobyl accident	0.002
Nuclear fuel cycle	0.0002

Source: UNSCEAR 2008 Chris Clement

CT scan optimization is used to reduce the patients' exposure to ionizing radiation.[4] In a study carried out by the Centre for d'expertise clinique en radioprotection (CECR) to evaluate the functionality of CT scanners (Figure 1), 56 systems were tested: 47% from GE, 28% from Siemens, 17% from Toshiba, and 8% from Philips. The optimized protocols by anatomy were 31% head exams, 37% chest exams, and 32% abdomen–pelvis exams. The optimized protocols reduced the patient

1 Lecomte R., Université de Sherbrooke. Dosimetry and radioprotection in preclinical molecular imaging: Current status and challenges.

2 See glossary on page 12.

3 Clement C. ICRP and IRPA. Advances in radiological protection in medicine.

4 Lemieux R, Rouleau M., Moulay AN. Centre d'expertise clinique en radioprotection (CECR), Centre hospitalier universitaire de Sherbrooke. Optimization of CT scan protocols to reduce patient exposure to ionizing radiation.

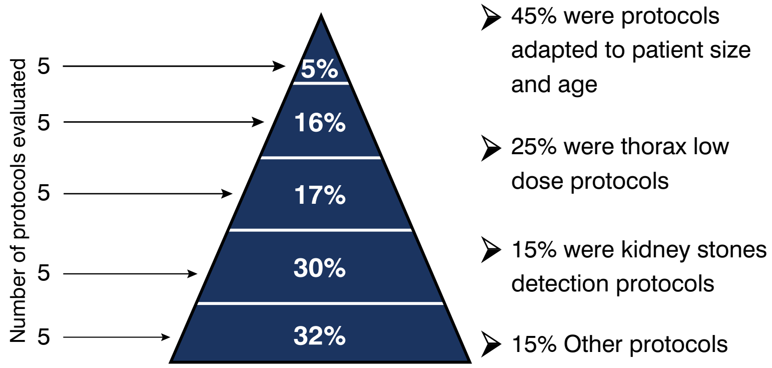

Figure 1: Non-standard optimized protocols in 37 out of 66 CT scans by CECR. (Source: Renald Lemieux)

Figure 2: Anthropomorphic phantom has geometry and composition very different from the cylinder. Differences between $CTDI_{vol}$ and actual patient dose can be more inaccurate when scanning children. (Source: Dr. Sylvain Deschenes)

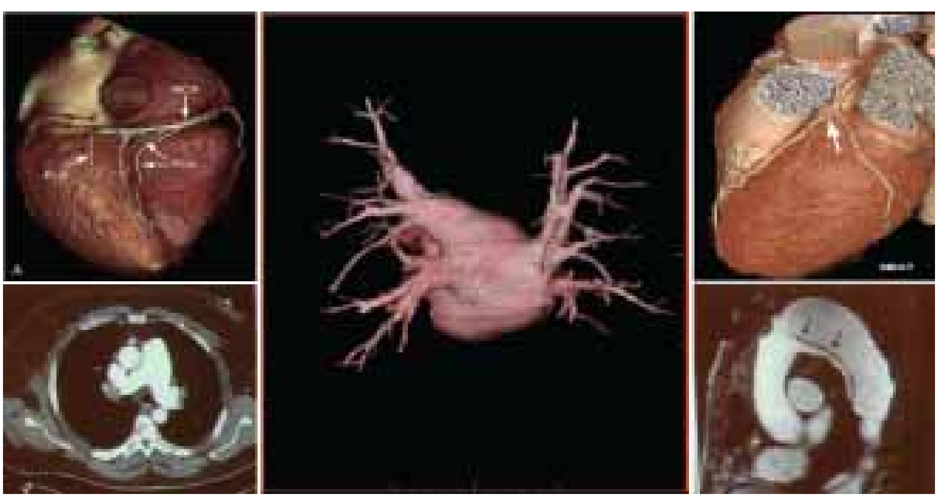

Figure 3: The great promise of multi-slice computed tomography was the "triple-rule-out." About 10% of patients with acute myocardial infarction are inappropriately discharged from the emergency department. (Source: Dr. Gerald Gahide)

dose by 18% to 24%, without degradation in image quality. The non-standard optimized protocols are shown in Figure 1. The ensuing recommendations are to use bismuth shielding as required, to use low-dose protocols for follow-up exams, and to be specific to children's size and age. The centre will continue visiting medical labs to further their procedures.

For better estimation of doses from CT scan examinations, size specific dose estimates (SSDE) is an alternative metric to report dose and to evaluate exposure in pediatric CT scans.[5] The dimensions of patients, such as children, are considered since these are not well-represented by phantoms (Figure 2). Comparisons were made between size-specific dose estimate (SSDE) and $CTDI_{vol}$[6] on 461 routine chest and 97 routine abdomen–pelvis examinations performed on pediatric patients over a period of 5 years. Compared to SSDE, $CTDI_{vol}$ underestimates the dose received for all abdomen–pelvis examinations, and for 91% of chest examinations. In summary, $CTDI_{vol}$ leads to false estimates and misinterpretation of the radiation dose from CT scans, whereas SSDE is easy to calculate offering a more accurate evaluation of dose. There is a weak correlation between a patient's age and dimensions, but they are less effective.

Non-invasive coronary angiography became feasible when the 16 slice CT scanners came into use in 2002 and promised the "triple-rule-out"[7] (Figure 3). However, the procedure delivered a higher dose to the patient than the invasive procedure, the margins being 10 to 20 mSv by MSCT scan and 3 to 6 mSv for the invasive technique.[8] Statistics show that between 1993 and 2006, the U.S. population grew by 1% annually, yet the use of CT scans increased by nearly 10%, and the effective dose increased by almost 600% from 0.5 mSv to 3 mSv (1980–2006). Following the ALARA principles, dose reduction methodologies were instituted, such as gantry rotation speed, the number of detectors, iodine concentrations, software modifications, that is, iterative reconstructions, and pharmacological protocols by beta blockers and nitric oxide. High-quality examinations can now be achieved with a radiation dose of 1 to 6 mSv.

The experiences at the Neonatal Intensive Care Unit at the University of

5 Deschênes S. CHU Ste-Justine, PQ. Use of size-specific dose estimates (SSDE) to report dose and evaluate exposure in pediatric CT scans.

6 See glossary on page 12.

7 See glossary on page 12.

8 Gahide G. Université de Sherbrooke. Cardiac CT and radiation safety: A Sherbrooke experience.

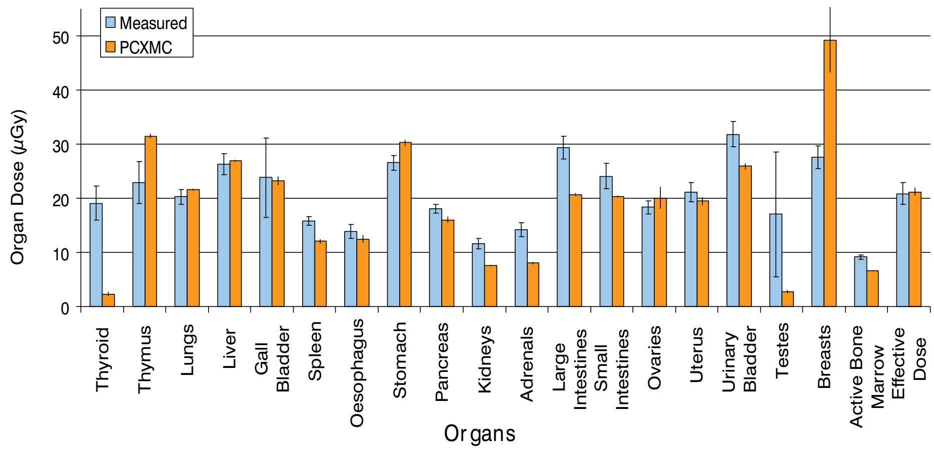

Figure 4: Measured and simulated organ doses. (Source: Dr. Elbakri)

Table 2: Excess dose contributed by impurities.

70 Kg Adult (740 MBg)	^{93}Tc	^{94}Tc	^{95}Tc	^{95m}Tc	^{96}Tc	^{99m}Tc	Total	% Excess Dose
	Dose (mSv)							
Effective Dose Equivalent	1.72E-02	6.29E-02	3.47E-02	1.84E-01	9.25E-02	5.23E+00	5.62E+00	6.96%
Effective Dose	2.53E-02	9.18E-02	4.88E-02	2.56E-01	1.24E-01	7.99+00	8.54E+00	6.39%
19 Kg Adult (740 MBg)	**^{93}Tc**	**^{94}Tc**	**^{95}Tc**	**^{95m}Tc**	**^{96}Tc**	**^{99m}Tc**	**Total**	**% Excess Dose**
	Dose (mSv)							
Effective Dose Equivalent	1.72E-02	5.86E-02	3.02E-02	1.77E-01	7.46E-02	6.55E+00	6.91E+00	5.18%
Effective Dose	2.63E-02	8.81E-02	4.37E-02	2.57E-01	1.03E-01	1.02E+01	1.07E+01	4.83%

Source: Svetlana Selinova

Manitoba were shared by Idris Elbakri.[9] In one study, the doses calculated from Monte Carlo simulation (using PCXCM 2.0 software) were compared with those from thermoluminescent dosimeter (TLD) measurements. The effective dose was 21.2 ±0.7 µSv (Monte Carlo) and 22.0 ±0.5 µSv (TLD). Whilst these measurements are in close agreement for effective dose, they varied widely for organ doses ranging from 85% for testes to 1.4% for the lungs. The study illustrated that PCXMC could also be used to estimate organ doses and effective doses for newborns. Measured and simulated organ doses are compared and shown in Figure 4 for various organs.

The most widely used isotope in nuclear medicine for imaging is ^{99m}Tc (meta-stable technetium), with 30,000 therapeutic scans per week in Canada, 400,000 in the United States, and 600,000 globally.[10] The process of generating ^{99}mTc begins with ^{100}Mo, an element that is mined and placed as targets in a nuclear reactor using highly enriched ^{235}U, with the end product being ^{99}Mo.

A technetium generator produces the ^{99m}Tc as follows:

$$^{99}\mathrm{Mo} \xrightarrow{\beta^-} {}^{99m}\mathrm{Tc} \xrightarrow{\gamma} {}^{99}\mathrm{Tc}$$

$$^{100}\mathrm{Mo}\,(p,2n)^{99m}\mathrm{Tc}$$

An alternate technology for producing ^{99m}Tc is needed in lieu of highly enriched uranium (HEU), and a cyclotron method is used to follow the ^{100}Mo (p,2n)^{99m}Tc process. One cyclotron per ½ million population could satisfy the ^{99m}Tc needs for Canada. Though the final imaging product obtained from either the reactor or from the cyclotron are equivalent, there are characteristic impurities to either method. Procedures to isolate ^{99m}Tc should be developed to remove ^{100}Mo/^{99}Mo as well as selected niobium isotopes impurities (reactor produced) and traces of non-^{99m}Tc isotopes (cyclotron produced). These contribute to additional radiation to patients because of their longer half-life (Table 2).

US Pharmacopoeia sets limits on these impurities to 0.015% of the ^{99m}Tc radioactivity, not to exceed 0.05% of other radionuclide impurities. The appropriate infrastructure (hot cells, bunkers, shielding, etc.) at cyclotron sites may need upgrading. Other means of producing ^{99m}Tc can be found in two articles in the Canadian Nuclear Society Bulletin (March 2011) 32(1): "Update on Radioisotopes and Nuclear Reactors" (p.15), and "Which Way Radioisotopes" (p.18), both authored by N. Sion.

The winner of the CRPA Student Contest, Aaron Chester,[11] gave a talk about the monitoring of rainwater and seaweed in British Columbia, Canada, to reveal the long-range transport of ^{131}I after the Fukushima nuclear accident. The release of ^{131}I from nuclear fission is about 2.89% of the fission yield of enriched uranium and is used as a prime indicator

9 Elbakri I. Cancer Care Manitoba, University of Manitoba. Striving for ALARA in the neonatal intensive care unit.

10 Selivanova S, Matei L, Dumulon-Perrault D, Rousseau J, Turcotte E, Guerin B, Lecomte R. CHUS, Université de Sherbrooke. Tc-99m pertechnetate production using a cyclotron.

11 Chester A. Simon Fraser University. Monitoring rainwater and seaweed in southwest and central British Columbia, Canada, reveals long-distance transport of I-131 following the Fukushima nuclear accident in Japan.

Table 3: Comparison of Dose Estimates for Residents in Fukushima, Chernobyl, and Canada

Location	Dose	Dose Limit
Chernobyl	~ 1 μSv	1 mSv/y
Fukushima	~ 0.1 μSv	1 mSv/y
Vancouver	1.3 mSv/y	----

The impact is negligible

Comparison With Global Locations for ^{131}I Monitoring

Location	Airborne [mBq/m³]	Rainwater [Bq/L]
Milano, Italy	0.46	0.89
Jeju, S. Korea	0.89	2.81
Bordeaux, France	2.36	3.50
Pacific N.W. North America	4.40	5.80 (at BC campus)

Source: Aaron Chester

Table 4: UV effects on the eye.

UV Type	Wavelength λ (nm)	Absorption % Cornea	Aqueous	Lens	Vitreous
UVc	< 280	100	0	0	0
UVb	300	92	6	2	0
	320	45	16	36	1
UVa	340	37	14	48	1
	360	34	12	52	2

Source: Annie Mercier

of nuclear incidents. Gamma ray spectroscopy was used in conjunction with an high purity germanium (HPGe) detector on collected rainwater at the Simon Fraser University's Burnaby campus, and it indicated a maximum ^{131}I activity of 5.8 Bq/L. The action level is 100 Bq/L, set for drinking water. Hence, the radiological impact on Canada is negligible (Table 3). On brown seaweed, the activity was 130 Bq/kg some 11 days after the accident, less in other areas of seaweed collection. This is an order of magnitude below the samplings after the Chernobyl accident. Hence, the impact of the Fukushima accident on the environment and on human health in Canada is insignificant.

Cell phones are in the category of non-ionizing radiation, 3 kHz to 3 GHz. A recent International Agency for Research on Cancer (IARC) classification of radiofrequency (RF), placed mobile (cell) phones in the 2B classification[12] Studies of population exposures from sources such as AM/FM/TV broadcast towers and from mobile phone base stations indicated that the exposures were below the limits.[13] But mobile phone use at the head is the most detrimental personal exposure. Mobile phones frequencies are shown in Figure 5.

Figure 5: Mobile phone frequencies. (Source: National Collaborating Centre for Environmental Health. (NCCEH))

The increasing number of sources, combined with increasing duration of use, is potentially increasing the total exposure to RF over time. Usage in motion, such as in a car or train, increases the power output, another detriment. Also, during data transfer power output is about four times higher. At resonance frequencies of 2100 and 2400 MHz, there is greater RF absorption by the skin. Methods to reduce exposure include a reduction in usage time, texting in lieu of calling, distancing the antenna from the head, turning off the phone when not in use, and using phones with lower specific absorption rate (SAR)[14] ratings.

There were two other presentations on non-ionizing radiation. Part 1 on UV radiation and light-emitting diodes (LEDs) by Annie Mercier[15] addressed radiation from mercury lamps, halogen and germicidal lamps, and LEDs and their risk to health. Table 4 shows the percentage absorption of UV by the eye where cataracts and lenticular opacities can be produced that are non-reversible. Other effects of overexposure include keratoconjunctivitis, but this effect heals within days.

LEDs are used because of their longer life (50,000 h versus 1000 h for the incandescent bulb), and their luminous efficiency of 100 to 150 Lumens/W, which is ten times higher than that for the incandescent light bulb. The detrimental effect on the eye is the accumulated dose on repeated low-intensity exposure and the photochemical damage on the retina (Figure 6 on p.7).

Radiation exposure to the lens of the eye is considered a deterministic effect by ICRP-60 (1990), causing opacity of the lens of the eye at a threshold of 5 Gy leading to cataracts.[16] Current dose limits are 150 mSv/y for a nuclear energy worker (NEW) and 15 mSv/y for the public. The latest epidemiological studies are to lower the threshold limits of absorbed dose by ten times to a threshold of 0.5 Gy. (ICRP statement 21 April 2011). ICRP has now recommended that the eye dose limits are not to exceed 20 mSv/y when averaged over five

12 Group 2B lists possible substances and exposures that are carcinogenic to humans.

13 Shum M. National Collaborating Centre for Environmental Health (NCCEH). Putting population exposures to radiofrequency-emitting sources into context.

14 See glossary on page 12.

15 Mercier A. Université Laval, Quebec. Universite Laval, Quebec. Part 1, Non-ionizing Radiation in Universities: Presence, Risk and Prevention at Université Laval. Ultraviolet radiation and light emitting diodes.

16 Gaw A. Canadian Nuclear Safety Commission. Proposed changes to the dose limit for the lens of the eye.

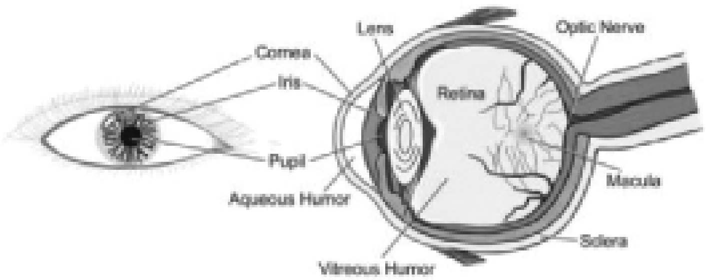

Figure 6: Composition of the eye. (Source: Annie Mercier)

Figure 7: Possible positioning of eye dosimeters. (Source: Adelene Gaw)

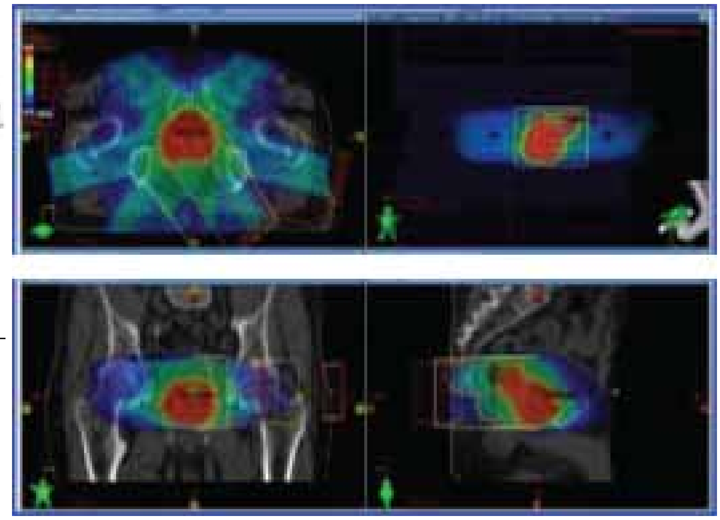

Figure 8: IMRT teatment of a 71-year-old male with adenocarcinoma of the prostate, preserving the rectum and bladder. (Source: M'hamed Bentourkia)

years with no single year exceeding 50 mSv. The Canadian Nuclear Safety Commission (CNSC) is proposing to adopt the new ICRP recommendations in the upcoming amendments to the Radiation Protection Regulations (RPRs). Standards are underway, with the International Electrotechnical Commission (IEC) (IEC 61331-3) expected by 2013–2014. There are currently no available standards for dosimeters measuring directional dose equivalent at a depth of 3 mm but theoretical work is being carried out by Physikalisch Technische Bundesanstalt (PTB) Germany to assess in what situations Hp(0.07) and Hp(10) could be an adequate alternate. New procedures are being developed and would be published by International Committee on Radiation Units (ICRU) and International Standards Organization (ISO) (ISO 15382).

Some dosimeters that are used in measuring are shown in Figure 7; however, their positioning may be impractical or uncomfortable. The International Atomic Energy Agency (IAEA) is due to publish a technical document (TECDOC) later in 2013, after member states have had an opportunity to comment on dose to the eye. Further publication of the related guide documents are due in 2015–2016.

To reduce fluoroscopy in cardiac diagnostic imaging procedures, MediGuide Technology™ is used.[17] It is an electromagnetic positioning system using 3-D tracking where devices, for example, catheters and wires, are equipped with MediGuide sensors to show position and orientation to an accuracy of 1mm and one degree. The system incorporates motion compensation to account for patient movement. Fluoro-free stenting is achievable and fluoro procedures have been reduced from 1.25 to 2 h to less than four minutes. The technology was approved by Health Canada in December 2012.

For an understanding of "nuclear" in nuclear medicine, M'hamed Bentourkia[18] presented an excellent workshop beginning with the basic structure of the atom, energy, and emissions, and the origin and interaction of radiation with matter including cellular. He then focused on the photons commonly applied in radiotherapy where ionization requires at least 13.6 eV and is applied to imaging. Such interactions produce X-rays, *bremsstrahlung*,[19] and gamma radiation, as well as one positron and one electron that annihilate to produce 2 x 511 keV gamma rays. The deposition of energy, that is, kerma[20] versus absorbed dose, was defined and illustrated. For organ weighting factors, ICRP-60 was used. Intensity-modulated radiation therapy (IMRT) is advocated where radiation doses are delivered with precision without harming the surrounding cells. This was achieved with 3-D CT scans or with MRI imaging in conjunction with dose calculations (Figure 8). The image clarity for a chest X-ray is also shown in Figure 9.

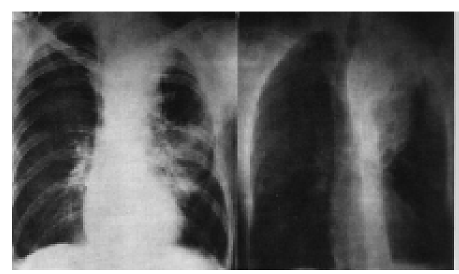

Figure 9: Chest X-ray by 80 kV (left) and 2 MV (right). (Source : M'hamed Bentourkia)

A scanner for small-animal imaging has been developed using fluorescence diffuse optical tomography (F-DOT).[21] It is capable of simultaneous multi-view tomographic measurements, and can obtain deep interior 3-D images of ≥ 1 cm of living organisms with non-invasive exterior-only measurements (Figure 10 on p.8). It uses light and optical techniques rather than

17 Soucie L. St-Jude Medical Inc. MediGuide technology.

18 Bentourkia M. Université de Sherbrooke. Interaction of radiations with matter. Also, Assessment of atherosclerosis in elderly with 18F-FDG-PET.

19 See glossary on page 12.

20 See glossary on page 12.

21 Bérubé-Lauzière Y. Centre d'imagerie moléculaire de Sherbrooke (CIMS), Université de Sherbrooke. Fluorescence diffuse optical tomography (F-DOT) for small-animal imaging.

Figure 10: Scanner with 7 dual wavelength non-contact fluorescence imaging. (Source: Yves Berube-Lauziere)

Table 5: Results of atherosclerosis tests.

Groups	Time 0	Time 12 m	p-value at 0.05
Calcified arteries N	1.80± 0.34	2.06±0.79	ns, p=0.285
Calcified arteries H	1.87± 0.26	2.07±0.36	ns, p=0.0782
Calcified arteries A	1.83± 0.25	1.86±0.24	ns, p=0.691
Non Calcified arteries N	1.10± 0,78	2.21±0.42	s, $p=1.23x10^{-11}$
Non Calcified arteries H	1.61± 0.27	2.16±0.52	s, $p=5.32x10^{-6}$
Non Calcified arteries A	1.50± 0.23	1.65±0.23	s, p=0.0216

Source: Dr. M'hamed Bentourkia

Table 6: Radon concentration and when measures are to be taken.

Radon Concentration	Recommended intervals between measurements
> 600 Bq/m3	Less than 1 y
Between 200 Bq/m3 and 600 Bq/m3	Less than 2 y
< 200 Bq/m3	No measures required

Source: Michel Deschamps

X-rays, magnetic fields, and/or ultra-sound imaging. The applications are in mammography (breast imaging), brain imaging, prostate imaging, joint arthritis, and *in vivo* small-animal imaging. The subject is placed on a 360° independently rotating table from the detectors. The scanner is comprised of a pair of stereo cameras for measuring the outer shape of the subject in 3D. Phantoms are used to validate the instrument.

Typically, biological tissue has distinct optical properties. Time-domain measurements with ultra-short pulses are injected into the medium using a Ti-sapphire laser system at additional cost, in lieu of laser diodes. Fluorescence is used, which means that where light is excited at a certain wavelength, it is re-emitted at a larger wavelength.

To reduce the dose to patients, Renald Lemieux et al.[22] of CECR have embarked on the design of a patient surveillance system with a data base that is accessible to all radiological departments and private clinics in Quebec. CECR is collaborating with Health Canada on the collection of CT scan data to define Canadian diagnostic reference levels.

Lucie Simoneau,[23] from the Operation Inspection Division (OID) of the CNSC, outlined the findings of 1500 inspections between 2010 and 2012, focusing on compliance performance in nuclear medicine. From this compilation, licensees can determine where they can improve their radiation protection program, and they are encouraged to do so.

Using lasers requires practical safety training[24] since accidents can have serious consequences that result in partial or total loss of vision. New users should become familiar with beam alignment techniques and search for the stray beams. Safety training includes how to keep the beam horizontal, avoid stray beams from mirrors and prisms, and optimize beam alignment using irises and fiber optic coupling, even if it is difficult to achieve.

To monitor atherosclerosis progression, a subject group aged 65 to 85 was sorted into thee classifications: normal (N); hypercholestrolemics (H), who were taking rosuvastatine medication; and angina (A), whose condition was stable by taking their prescription medicine. They were tracked over a period of 12 months for atherosclerosis, that is, plaque in their aorta and iliac arteries, using CT and PET imaging.[25]

The results in Table 5 show an increase in arterial inflammation in group H, despite them taking rosuvastatine. In summary, analyses with ^{18}F-FDG-PET/CT could be efficient, though expensive, in localizing atherosclerosis and monitoring its progress instead of by global evaluations with systemic biomarkers.

Radon is a natural phenomena in the Earth's crust, and its concentration has the potential risk of inducing lung cancer. Radon begins its life from ^{238}U and through successive decays becomes Lead-210 (Figure 11). Lung cancer risk is 1:20 for non-smokers in an elevated radon environment but 1:3 for smokers.[26] It was recommended in 2007 that environmental radon should be < 200 Bq/m^3. Table 6 shows the radon concentrations at which measures are to be taken. The recently formed Canadian Association of Radon Scientists and Technologists has a certification program for measurement and mitigation of radon.

It is increasingly accepted that microenvironment plays a part in tumour progression and that inflammation is associated in promoting metastasis[27] so that radiation-induced inflammation in a healthy breast could stimulate the migration of cancer cells to form metastases. To verify this hypothesis, the mammary glands of a Balb/c mouse were irradiated with four fractions of 6 Gy at 24 h intervals using a Gamma Knife. The glands were then implanted with D2A1

22 Lemieux R, Rouleau M, Moulay AN. Centre d'Expertise Clinique en Radioprotection (CECR). Role of the CECR in the appropriation of a standardized practice in radiation protection in Quebec.

23 Simoneau L. CNSC. Compliance performance overview of nuclear substance licenses and a review of new initiatives within the CNSC compliance program.

24 Sonoc S. University of Toronto. Laser safety training.

25 Bentourkia M. Université de Sherbrooke. Interaction of radiations with matter. Also, Assessment of atherosclerosis in elderly with 18F-FDG-PET.

26 Deschamps M. Quebec Radon Inc. Radon in Canada and particularly in Quebec.

27 Paquette B, Bouchard G, Therriault H, Bujold R, Saucier C. Université de Sherbrooke. Pre-irradiation of mouse mammary gland stimulates the migration of breast cancer cells.

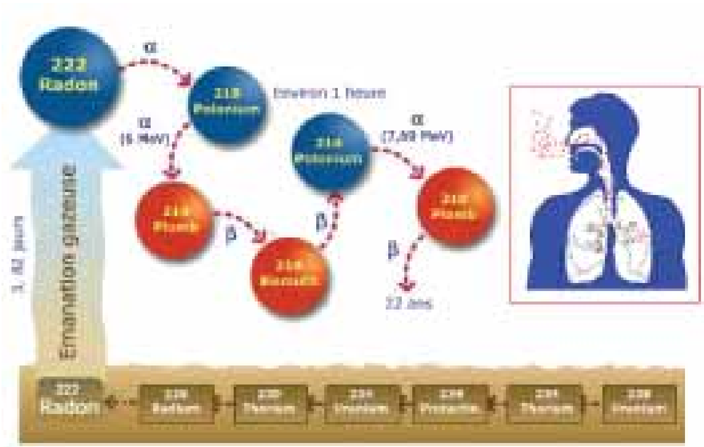

Figure 11: Decay pathway leading to radon. (Source: Michel Deschamps)

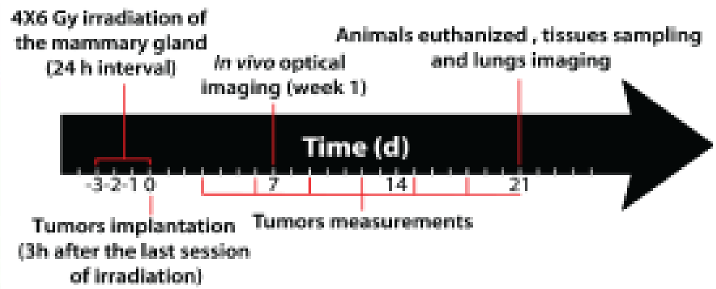

Figure 12: Enhancement of cancer cell invasion in vivo of Balb/c mouse. (Source: Benoit Paquette)

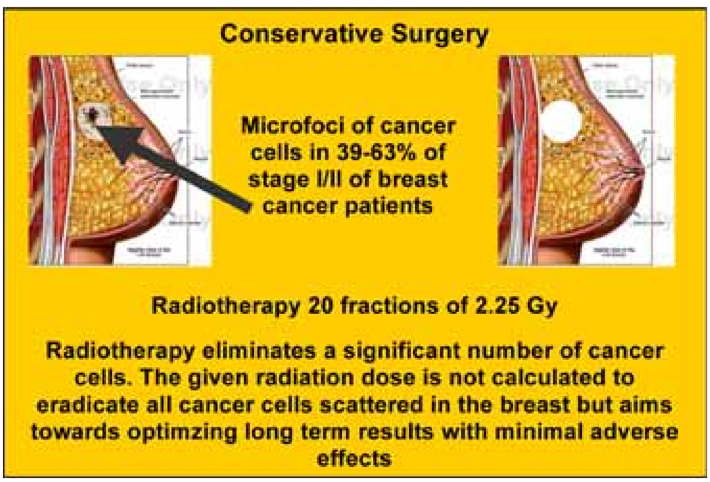

Figure 13: Current breast cancer treatment. (Source: Dr. Benoit Paquette)

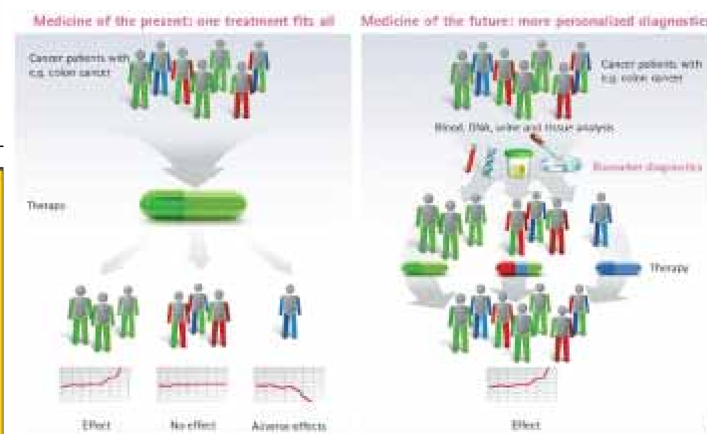

Figure 14: The case for personalized medicine (e.g., colon cancer treatment). (Source: Dmitry Klokov et al)

FUCCI-labelled breast cancer cells close to the nipple and tracked (Figure 12). The pre-irradiation increased the migration and quantity of cancer cells and the number of lung metastases. These adverse effects are attributed to the induction of pro-inflammatory molecules such as COX-2 and IL-6. However, in conservative surgery using radiotherapy, the aim is at optimizing the long-term results rather than eradicating all cancer cells, (Figure 13). Therefore, an alternative approach is proposed by targeting the pro-migratory molecules triggered by radiation to increase disease-free survival in TNBC (triple negative breast cancer) patients.

Exposure to ionizing radiation (IR) is known to damage the DNA by causing genetic alterations, the likely route to cancer.[28] The DNA repair pathways are quite complex, particularly in double-strand breaks, and may follow any of these repair mechanisms: homologous combination, mismatch repair, nucleotide exclusion repair, DNA strand crosslink repair, and/or non-homologous end joining. The key regulating and well-known molecules are the H2AX, ATM, and the p53 proteins. However, there is a new candidate: Foxo3A transcription factor. It is of interest whether there is a link between H2AX and Foxo3A. Tests on genetically matched mice showed that H2AX plays a role in the Foxo3A-regulated stress response, whose deficiency would cause genomic instability and radio sensitization. This may potentially be used in nuclear medicine for screening radio-sensitive individuals and thus makes a case for personalized medicine (Figure 14), where persons would have their genome sequenced. Ethical issues would ensue.

There are four Gamma Knife devices that have been in service in Canada since 2004, one of which resides at the Centre Hospitalier Universitaire de Sherbrooke,(CHUS),[29] which performs about 400 treatments per year. The treatments are for certain tumours, vascular malformations, and functional disorders. One hundred and ninety-two collimated ^{60}Co sources are used to deliver focused radiation to the tumour, sparing the surrounding healthy tissue. At the machine, the patient receives 8 Sv/h limited to the head area at the tumour. This is, of course, less invasive than traditional surgery. Each treatment is individualized and requires a multidisciplinary team of medical physicists, neurosurgeons, oncologists, nurses, and technologists.

28 Klokov D, Bhardwaj T, Tarrade S. Chalk River Labs, AECL. The role of H2AX in the Foxo3A-regulated molecular pathways elicited in the response to ionizing radiation exposure.

29 Delage P. Centre Hospitalier Universitaire de Sherbrooke. Clinical usage of Gamma Knife at the CHUS.

Table 7: Comparison of internal exposure pathways and limits.

Isotope	Half Life $\tau^{1/2}$ h	Ingestion Effective Dose mSv/MBq (Limit 1 mSv)	Inhalation Effective Dose mSv/MBq (Limit 1 mSv)	Integrated Skin Dose Per 1 cm² mSv/MBq (Limit 500 mSv)
^{13}N	0.17	0.016	0.013	460
^{11}C	0.34	0.024	0.002	900
^{18}F	1.83	0.049	0.093	4600
^{64}Cu	12.70	0.120	0.150	18000
^{124}I	100.30	13.0	6.3	75000

Source: Adam Dodd, CNSC Workshop What is a dangerous level of contamination?

Figure 15: Cyclotron beam line. (Source: CHUS Facility)

Figure 16: PET animal scanner. (Source: CHUS Facility)

Figure 17: Hot cell. (Source: CHUS Facility)

Figure 18: Gamma knife, the Leksell PERFEXION Elektra. (Source: CHUS Facility)

Linear accelerators are housed in bunkers, and bunkers need to be licensed. Both robotic and tomographic accelerators need a CNSC license to construct, operate, and finally, to decommission.[30] The previous photon energy exemptions of 10 MeV have now been reduced to 1 MeV. Regulatory requirements on the effects of neutrons are increasingly stringent. Construction and shielding are built to handle photon and electron radiation at the designed maximum energy levels, also taking into consideration primary and secondary radiation via scatter and leakage, and the protections aim for a dose of 1 mSv/y for a NEW (Nuclear Energy Worker) and 50 µSv/y for the general public. At the primary and/or secondary walls, the instantaneous dose rate (IDR) is < 25 µSv/h and the TADR (time-averaged dose rate) is at < 20 µSv/h. These follow the National Committee for Radiation Protection (NCRP) guides.[31]

The cyclotron workshop given by the CNSC covered facility design, operational safety, and shielding by using Monte Carlo simulations, but its primary focus was on ^{99m}Tc isotope production in order to diversify the supply of ^{99m}Tc. It is intended that one cyclotron will be available per half-million Canadians. There are a number of issues to consider: licensing, target room and shielding design, hot cells and their ventilation, and possible spillage. Due to the nature of cyclotron operation there are cautions to be taken such as target failure, emission of $^{11}CO_2$ from the ventilation stacks, vault airtight seals leakage, and air activation due to neutron capture by the argon in the air. The exposure pathways that may incur are shown in Table 7.

Cyclotron challenges during the commissioning of the TR24 Cyclotron at CHUS were highlighted,[32] where primary barrier failure, high activation in the cooling system and vault, and radioactive dust from the ^{99m}Tc target transfer system were encountered. These were overcome so that the dose rate leaking under the door was reduced to 1.5 µSv/h gamma and 59.3 µSv/h neutron. The cyclotron uses 24 MeV protons and 500 µA, and has two beam lines for two targets (Figure 15). Radiopharmaceutical isotopes produced are ^{18}F, ^{60}Cu, ^{61}Cu, ^{64}Cu, ^{89}Zr, and ^{99m}Tc. CHUS also has a LabPet, SPECT-CT, and PET scanners (Figure 16).

Similar issues were encountered at the PET cyclotron facility at McMaster University,[33] where the following positron-emitting radionuclides are produced: ^{18}F, ^{11}C, and the novel imaging agent ^{124}I. Cooling system failure occurred with beam currents of 20 µA.

A visit to the CHUS ensued, hosted by Roger Lecomte and CHUS staff to view their equipment (Figures 15 to 18). The facility can treat 24 patients daily. There is a Philips Gemini scanner with epidemiological studies on magnets that rotate 3/s; it also uses a ^{64}Cu tracer. This tracer resides about 7 h in the patient. PET scanners for animals are also used to develop

30 Evans M et al. McGill University Health Centre. Linear accelerator bunker design, construction and management in a hospital setting (1983–2013).

31 NCRP-151, Radiation Protection in the Design of Radiotherapy Facilities.

32 Mercure S. CHUS. Challenges encountered during a cyclotron installation at the CHUS.

33 Moscu D. McMaster University. Preliminary experience of research activities at a PET cyclotron facility.

a protocol of transferring the amounts of tracers to humans, using a proportionate conversion factor. Rats are injected with $Na^{18}F$ that never leaves the body of the animal and compared to another animal with ^{11}C acetate, ^{11}C methionine, and ^{11}C FDG (fluorodeoxyglucose) to check on tumour response (for example, bone metastatic prostate cancer) after photo dynamic therapy. Among the advanced equipment that CHUS has is the Gamma Knife (Figure 18). Patients must have an MRI to fix the position of the tumour before being treated. A precisely collimated beam is then focused to an accuracy of 0.5 mm. Treatments are calculated for individual patients and last about 30 min.

Acronyms

ACGIH	American Conference of Governmental Industrial Hygienists
AECL	Atomic Energy of Canada Limited
ALARA	as low as reasonably achievable
AM	amplitude modulation
CECR	Centre d'expertise clinique en radioprotection
CI	confidence interval, an indication of the reliability of an estimate
CHUS	Centre hospitalier universitaire de Sherbrooke
CNSC	Canadian Nuclear Safety Commission
CT	computed tomography
EMF	electromagnetic fields
eV	electron volt, a unit of energy equal to approximately $1.602176565 \times 10^{-19}$ Joule.
FM	frequency modulation
HEU	highly enriched uranium, usually U-235, a fissionable material
HPGe	high purity germanium detectors
IAEA	International Atomic Energy Agency, the nuclear watch-dog in Vienna
IARC	International Agency for Research on Cancer.
ICRP	International Commission on Radiological Protection
ICRU	International Committee on Radiation Units
IDR	instantaneous dose rate
IEC	International Electrotechnical Commission
IMRT	intensity-modulated radiation therapy
ISO	International Standards Organization
IRPA	International Radiation Protection Association
kerma	*k*inetic *e*nergy *r*eleased in *ma*terial (per unit mass)
LED	light-emitting diodes
MRI	magnetic resonance imaging
NCRP	National Committee for Radiation Protection
NEW	nuclear energy worker
PET	positron emission tomography
PTB	Physikalisch Technische Bundesanstalt is the highest standards laboratory in Germany.
RF	radiofrequency
SPECT	single-photon emission computed tomography
SAR	specific absorption rate
SSDE	size-specific dose estimate
TADR	time-averaged dose rate
TLD	thermoluminescent dosimeter

Glossary

Bremsstrahlung

A term from German meaning “braking radiation.” It is electromagnetic radiation produced when a charged particle decelerates or is deflected by another charged particle, typically an electron by an atomic nucleus where the particle decelerates and the other accelerates. The loss/gain in kinetic energy is converted into photons. This phenomena is the basis of synchrotron and cyclotron operation.

CTDIvol

The volume computed tomography dose index (CTDI) is the measure of ionizing radiation exposure per slice of data acquisition. The CTDIvol is calculated as [(NxT)/I] x CTDIW where N = number of axial scans per X-ray source rotation; T (tesla) = scan thickness in mm; I = table increment per axial scan in mm; CTDIw = average CTDI given across the field of view.

kerma

The *k*inetic *e*nergy *r*eleased in *ma*terial (per unit mass) and is the sum of the kinetic energies of the charged particles that are released by uncharged ionizing particles, such as photons and neutrons. Its unit is Joule/kg (i.e., Gray) the same as for absorbed dose, yet differs from absorbed dose at the higher energies because some of the energy is released from the absorbing material as *bremsstrahlung* X-rays for the fast moving electrons.

LD 50/30

The radiation dose expected to cause death to 50 percent of an exposed population within 30 days. For humans the dose is in the range of 4–5 Sieverts received over a very short period.

p-value

The probability of obtaining a test result as extreme as the one observed assuming the null hypothesis is true (that there is no relationship between the two phenomena) or when the value is less than the predetermined significant level of p = 0.05.

SAR

Specific absorption rate (SAR) is a measurement of how much electromagnetic radiation is absorbed by body tissue. Recommended limits of 2.0 W/kg in 10 g of tissue have been adopted in the UK, whilst the US adopted 1.6 W/kg in 1 kg of tissue

Triple-rule-out

In CT scans this was assumed to be appropriate because its MSCT “promised” reduced dosage for patients who were judged to be at low to intermediate risk for acute coronary syndrome and whose symptoms may also be attributed to acute pathologic conditions of the aorta or pulmonary arteries.

Biography

Nicholas Sion was employed at Ontario Power Generation (OPG) for about 28 years designing radiation monitoring instrumentation and reactor control. His discriminating tritium monitor, stack monitor, and C-14 monitor designs are operational at OPG and at Bruce Power. Sion was also a consultant at Atomic Energy of Canada Limited (AECL) for two and a half years on the MDS Nordion Medical Isotope Reactor (MMIR) MAPLE project.

Nicholas Sion a œuvré auprès de Ontario Power Generation (OPG) pendant environ 28 ans dans la conception d’instruments de surveillance des rayonnements et dans le contrôle de réacteurs. Ses conceptions discriminantes d’appareils de surveillance du tritium, de surveillance de faisceau, de surveillance du C-14 sont à l’oeuvre chez l’OPG et chez Bruce Power. Sion a aussi joué le rôle de conseiller auprès de Énergie atomique du Canada limitée (EACL) pendant deux ans et demie sur le projet MAPLE de MDS Nordion destiné à la production d’isotopes à des fins médicales (MMIR).