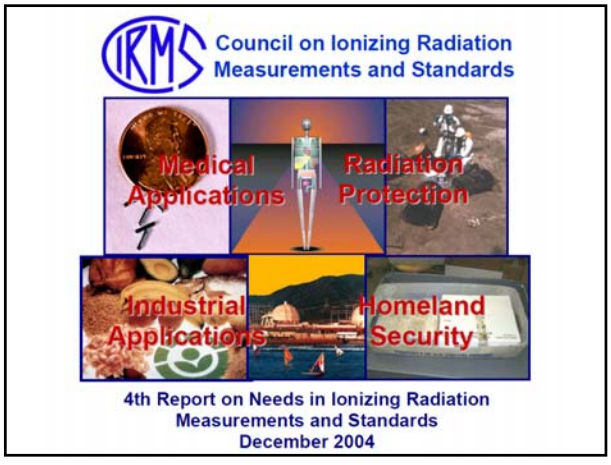
Randall S. Caswell Award

for Distinguished Achievements in the Field of Ionizing Radiation Measurements and Standards

2002	**H. Thompson Heaton II**	Center for Devices and Radiological Health, US FDA
2004	**Anthony J. Berejka** Ionicorp	
2006	**Kenneth L. Swinth**	Swinth Associates
2007	**Bert M. Coursey**	U.S. Department of Homeland Security
2008	**Larry A. DeWerd**	University of Wisconsin
2009	**Marshall R. Cleland**	IBA Industrial, Incorporated
2010	**Geoffrey Ibbott**	MD Anderson Cancer Center
2011	**Kenneth Inn**	NIST
2012	**Joseph C. McDonald**	Pacific Northwest National Laboratory, retired
2013	**Stephen M. Seltzer**	NIST
2015	**X. George Xu**	Rensselaer Polytechnic Institute

FIRST MEETING: JUNE 17, 1991

1991	Organizing Committee held 2 meetings On June 17 proposed a slate of officers
1992	Ballots mailed to participants in Organizational Meeting. Officers elected February 10
1992	Officers and Organizing Committee meeting March 31. CIRMS turned over to officers
1992	Invitations to join sent in April 10 organizations, corporations, and individuals
1992	Inaugural Meeting scheduled for October 22-23



January 21, 2004

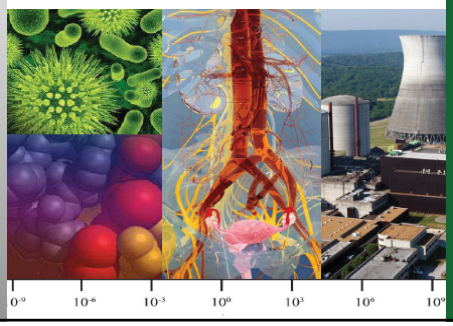
Dr. James Deye
National Cancer Institute
6130 Executive Blvd., MSC 7440
Rockville, MD 20892-7440

Dear Dr. Deye:

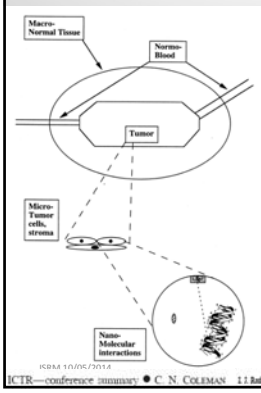
I would like to congratulate you on yet another successful annual meeting of the Council on Ionizing Radiation Measurements and Standards (CIRMS), held recently here at the National Institute of Standards and Technology. The focus of this latest meeting, "Radiation Radioactivity Measurements and Standards in Industry," clearly aligns with NIST's mission to "work with industry to develop and apply technology, measurements and standards." It is great to have so many representatives from the user

Arden L. Bement, Jr.
Director

A Matter of Scale:
PRECISION MEDICINE
from the Nano to the Giga



CANCER BIOLOGY – Nano to Giga



range and domains of radiation oncology sciences research:

The Macro-environment is the **normal tissue surrounding** *the* patient

The Normo-environment refers to **that which we see and measure in the clinic**.

The Microenvironment focuses on the **cellular environment** of the tumor but also includes the normal cellular component of a tumor—stromal, epithelial, vascular, immunologic,and inflammatory cells

The Nano-to-pico environment includes molecular targets and the many biochemical and molecular processes that occur within the cancer cell before, during, and after perturbation with radiation.

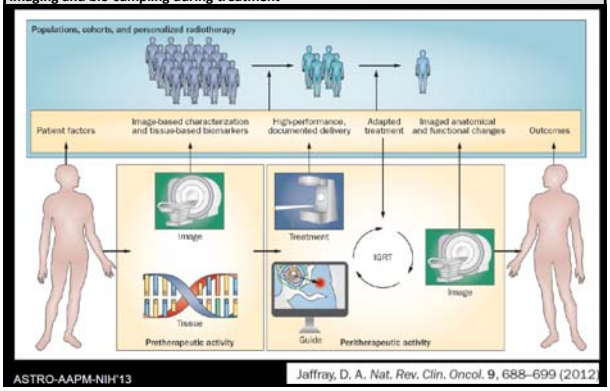
ICTR—conference summary • C. N. Coleman

PRECISION MEDICINE

- refers to the tailoring of medical treatment to the **individual characteristics of each patient**. It is based on the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease, in the biology and/or prognosis of those diseases they may develop, or in their response to a specific treatment

MEDICAL PRACTICE	OUTCOME	SCIENCE
Population	population **Average** no- / partial-/ complete-response	histo-path/ anatomy epidemiology/ statistics
Personalized	**Prognostic** likely course based upon pre-Tx "omics"	above + molecular biology
Precision	Predictive / **Quantitative** patient specific outcome / adaptive Tx	above + physics and chemistry of disease process

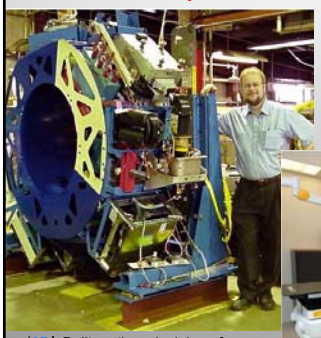
PM leads to tailoring of RT to the individual characteristics of each patient, based on the ability to classify individuals into subpopulations that differ in their tumor and normal tissue response to radiation based upon their "omics" and phenotype and as demonstrated by imaging and bio-sampling during treatment



ASTRO-AAPM-NIH'13

Jaffray, D. A. *Nat. Rev. Clin. Oncol.* **9**, 688–699 (2012)

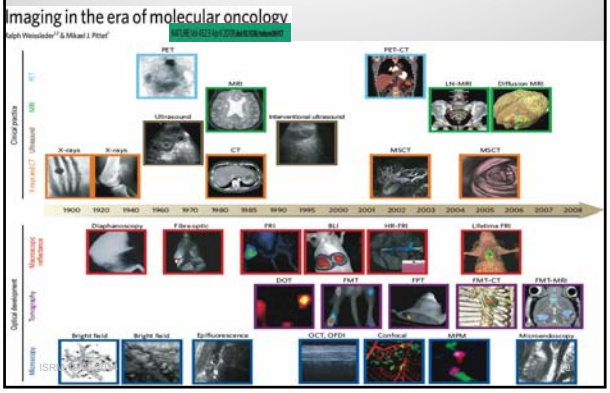
"anatomy based" RADIOTHERAPY



'4D' Gimballed linac "VERO" by Brainlab (Intra-Tx imaging)

'3D' Built on the principles of back projected CT

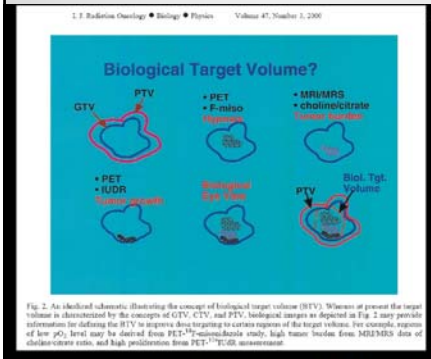
IMAGING SCIENCE



IMAGING STANDARDS

Quantitative imaging is an important method by which the distinctions among patients can be measured. Coupled with molecular profiling methods, quantitative imaging can become an important tool for stratifying patient characteristics for appropriate interventions

INTEGRATING FUNCTIONAL/MOLECULAR IMAGING



"Incremental to the concept of gross, clinical, and planning target volumes (GTV, CTV, and PTV), we propose the concept of "biological target volume" (BTV) and hypothesize that BTV can be derived from biological images and that their use may incrementally improve target delineation and dose delivery." - Ling et al.

Ling et al., Int. J. Radiation Oncology Biol. Phys., Vol. 47, No. 3, pp. 551–560, 2000

"biology based" RADIOTHERAPY

NOTE:

PRECISE DELIVERY of radiation Is NOT sufficient for PRECISION MEDICINE

Hypothesis: Patterning radiation dose according to imaged functional or molecular distributions will increase the TR

RADIATION SCIENCE AND MEDICINE

RELATED SESSIONS

AACR.org

MEET THE EXPERT SESSION
Radiation and Immunotherapy: From Preclinical Models to Cancer Patients
Tuesday, April 21, 2015, 7:00 a.m. - 8:00 a.m.
Room 108, Pennsylvania Convention Center
CME-Designated
Silvia C. Formenti. New York University, New York, NY

POSTER SESSIONS
Special Populations, Supportive Care, and Survivorship Research / Radiation Oncology
Tuesday, April 21, 2015, 8:00 a.m. - 12:00 noon
Section 23

Targeting Cell Death and DNA Repair
Tuesday, April 21, 2015, 8:00 a.m. - 12:00 noon
Section 32

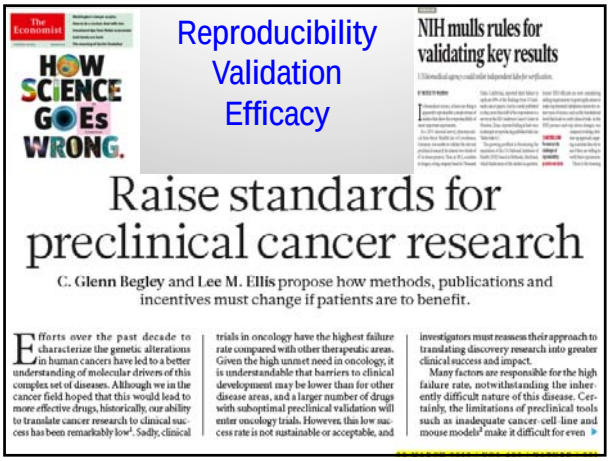
Radiation Biology 1: DNA Damage and Repair, Molecular Modulators of Radiation Response, and Resistance
Tuesday, April 21, 2015, 8:00 a.m. - 12:00 noon
Section 18

Radiation Biology 2: Modifiers and Signal Transduction, Sensitivity, Resistance, and Therapy

QUALITY ??

A recent review of the literature by Stone et al[1] found **significant concerns with preclinical data concerning the efficacy of 10 drug-radiation combinations presented in 125 publications prior to 2015.** While the preponderance of concerns were related to the biological aspects of these studies, it was also noted that necessary **radiation parameters were either "not reported (or were unclear-)" to an extent that compromised the reproducibility of the experiment**. This was true for both the in vitro and in vivo studies.

Stone H, Bernhard EJ, Coleman CN, et al. Systematic Review: Preclinical Data on Efficacy of 10 Drug-Radiation Combinations: Evaluations, Concerns and Recommendations. *Translational oncology.* 2015; in press.



Small animal radiotherapy research platforms

- F. Verhaegan et al, PMB 56 (2011) pp 55-83

R66 Topical Review

Table 2. Characteristics of small animal radiation research systems for rodents. All devices are based on x-ray tubes except the Washington University system which is based on an ^{192}Ir brachytherapy source.

System	Photon energy range (keV)	Field range at treatment site	Fixed fields/ arcs	Max dose rate (Gy min^{-1})	Image resolution at treatment site (μm)	Targeting accuracy (μm)	Refs
SARRP (Johns Hopkins University)	5–225	0.5 mm⌀–10 × 10 cm^2	F/A	4	130	200	Wong *et al* 2008, Tryggestad *et al* 2009, Matsufuji *et al* 2009
X-RAD (Princess Margaret Hospital)	5–225	1 mm⌀–10 × 10 cm^2	F/A	4	200	200	Clarkson *et al* 2010
Washington University (^{192}Ir)	380[a]	5–15 mm⌀	F	2.9	N/A	100–180[a]	Stojadinovic *et al* 2006, 2007, Kiehl *et al* 2008
Stanford University	70–120	0.1–6 cm^2[a]	F/A	2	49	100	Graves *et al* 2007, Rodriguez *et al* 2009, Zhou *et al* 2010
University of Texas Southwestern	5–320	1–20 mm⌀	F/A	>10	113	65	Song *et al* 2010, Pidikiti *et al* 2011

[a] Mean photon energy of gamma rays.

DOSE IS NOT JUST A NUMBER !

Volume 118 (2013) http://dx.doi.org/10.6028/jres.118.021
Journal of Research of the National Institute of Standards and Technology

The Importance of Dosimetry Standardization in Radiobiology

Marc Desrosiers[1], Larry DeWerd[2], James Deye[3], Patricia Lindsay[4], Mark K. Murphy[5], Michael Mitch[1], Francesca Macchiarini[6], Strahinja Stojadinovic[7], and Helen Stone[3]

1 National Institute of Standards and Technology, Gaithersburg, Maryland 20899
2 University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin
3 National Cancer Institute, National Institute of Health, Bethesda, Maryland
4 Princess Margaret Hospital, University of Toronto, Toronto, Ontario, Canada
5 Battelle–Pacific Northwest National Laboratory, Richland, Washington
6 National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
7 University of Texas Southwestern Medical Center Dallas, Texas

http://www.nist.gov/pml/div682/grp02/dosimetry-standardization-for-radiobiology.cfm

RT is "FOCUSED BIOLOGY"

We need to be aware that **when radiation interacts with cells** (tumor or normal) it

Not only effects that cell but it causes the release of molecules

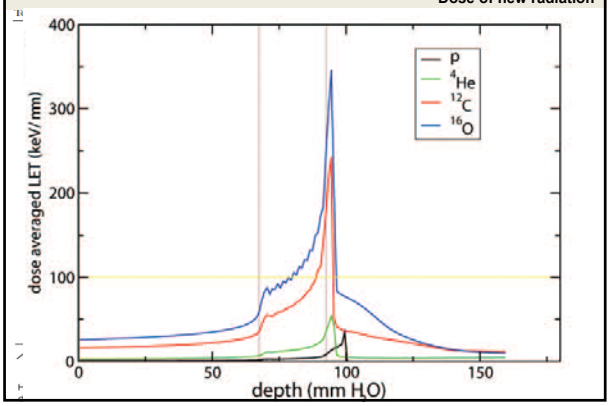
So we have a
(D, B) ➡ B*

but

(xD,B) ➡ B** ≠ xB*

C. Norm Coleman ITCR 2000 Conf Summary

But **dose is only a SURROGATE for biological effect** and lot of the underlying biology is unknown,so RT defines the **Relative Biological Effect: (RBE) = Dose of ref radiation / Dose of new radiation**



REVIEW ARTICLE Br J Radiol 2015;88: 20140392.

Future development of biologically relevant dosimetry

1,2H PALMANS, PhD, 3H RABUS, PhD, 4A L BELCHIOR, PhD, 3M U BUG, MSc, 1S GALER, PhD, 3U GIESEN, PhD, 5G GONON, PhD, 5G GRUEL, PhD, 3G HILGERS, PhD, 6D MORO, PhD, 3H NETTELBECK, PhD, 7M PINTO, PhD, 8A POLA, PhD, 9S PSZONA, PhD, 1G SCHETTINO, PhD, 1P H G SHARPE, PhD, 10P TELES, PhD, 5C VILLAGRASA, PhD and 11J J WILKENS, PhD

1Acoustics and Ionising Radiation Division, National Physical Laboratory (NPL), Teddington, Middlesex, UK
2Medical Physics, EBG MedAustron GmbH, Wiener Neustadt, Austria
3Abteilung Ionisierende Strahlung, Physikalisch-Technische Bundesanstalt (PTB), Braunschweig, Germany
4Associação do Instituto Superior T´ecnico para a Investigação e Desenvolvimento (IST-ID), Lisboa, Portugal
5Unit´e Radioprotection de l'Homme, Institut de Radioprotection et de S´uret´e Nucl´eaire (IRSN), Fontenay-aux-Roses, France
6Laboratori Nazionale di Legnaro, Istituto Nazionale di Fisica Nucleare, Padova, Italy
7Centro Ricerche Casaccia, Istituto Nazionale di Metrologia delle Radiazioni Ionizzanti ENEA-INMRI, Rome, Italy
8Department of Energy, Politecnico di Milano, Milan, Italy
9Kierownik Zatladu Interdyscyplinarnych Zastosowań Fizyki, Narodowe Centrum Bad´an Ja¸drowych, Otwock-Swierk, Poland
10Unidade de Protecção e Segurança Radiol´ogica, Instituto Tecnol´ogico e Nuclear, Instituto Superior T´ecnico, Sacav´em, Portugal
11Department of Radiation Oncology, Technische Universit¨at M¨unchen, Klinikum rechts der Isar, Munich, Germany

Given the complexity of the initiation and occurrence of biological processes on various time and length scales, and given that neither microdosimetry nor nanodosimetry on their own can fully describe the biological effects as a function of the distribution of energy deposition or ionization, a multiscale approach is needed to lay the foundation for the aforementioned new physical quantities relating track structure to relative biological effectiveness in proton and ion beam therapy.

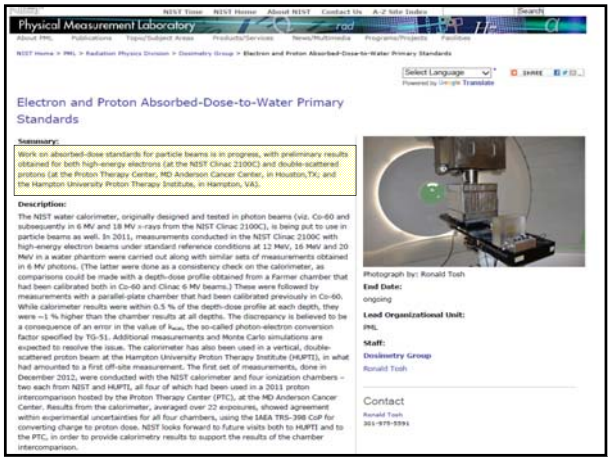
OPENMED Beam specification parameters (2016)

A proposal to transform an existing heavy ion accelerator at CERN, LEIR, into a non-clinical, biomedical research facility.

3.1.9 Requirements for dosimetry and fluence monitoring

Dose measurements must be possible at low and high dose rates, as well as for low and high LET particles.

• Basic dosimetry: ionization chambers and other techniques, solid state, calorimetry and chemical systems, as required in a medical clinic. This needs to be the **same standard as required by** Swiss/French **national reference laboratories for absorbed doses.**



Radiation Biodosimetry Medical Countermeasure Devices

Guidance for Industry and Food and Drug Administration Staff

Precision Medicine for Triage

Document issued on April 18, 2016.

The draft of this document was issued on December 30, 2014.

1. Accuracy in relation to the dose delivered

In order to demonstrate analytical accuracy, if the device output is radiation dose, then the device's measurement of the biological response to radiation will probably be compared to the physical calculated dose delivered. Therefore, the accuracy of the delivered dose is crucial, and the protocol for designing proper telemetry should be included in all study protocols. As discussed above, we expect that because the biodosimetry output will be confounded by the biological response to radiation, there will be between-individual variations which may complicate the correlation of the output to the radiation dose delivered.

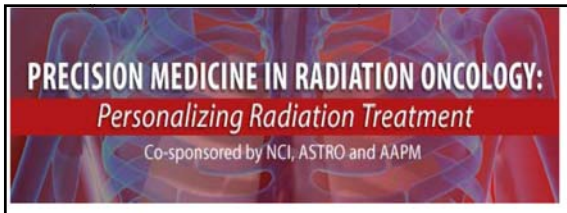
Precision Medicine (RT) > Radiation Standards

Physical dose for EBRT
(continuation – dosimeters, small fields)

Physical dose for pre-clinical and triage
(continuation – SOPs, counter measures (neutrons))

Physical dose for particle beams
(further development – measurements and basic reference data)

Activity Standards
(further development – clinical isotopes, QI/radiomics)



June 16-17, 2016

NIH Campus, Bethesda, Maryland

Message from the Director, NIH: Selection of Eric Dishman as Director of the Precision Medicine Initiative Cohort Program 4/12/2016

MUSEUM

NATIONAL INSTITUTE OF STANDARDS AND TECHNOLOGY

X RAYS

Radio Activity

Historical Standards

Working Standards

Measures of Gravity

NIST and The Nobel

---much more

Research in radium began at the National Bureau of Standards (NBS) in December, 1913 when a phial containing 20.28 milligrams of pure radium arrived from abroad. It was a certified equivalent to the International Radium Standard at Sevres, France, and a cover communication described its comparison with another quantity of radium salts prepared at Vienna and accepted as a second standard. NBS served hospitals and physicians by analyzing their radium salts against the international standard. Ernest Dorsey was the principal NBS researcher on radium as he made intercomparisons of sealed radium standards and started an investigation of the gamma-ray method of radium measurement. [From: Measures for Progress by Rexmond C. Cochrane, p. 146-147]

844 Sitzung der physikalisch-mathematischen Klasse vom 25. November 1915

Die Feldgleichungen der Gravitation.

Von A. Einstein.

In zwei vor kurzem erschienenen Mitteilungen[1] habe ich gezeigt, w
man zu Feldgleichungen der Gravitation gelangen kann, die dem Post
lat allgemeiner Relativität entsprechen, d. h. die in ihrer allgemein
Fassung beliebigen Substitutionen der Raumzeitvariabeln gegenüber k
variant sind.

Der Entwicklungsgang war dabei folgender. Zunächst fand i
Gleichungen, welche die Newtonsche Theorie als Näherung enthal
und beliebigen Substitutionen von der Determinante 1 gegenüber
variant waren. Hierauf fand ich, daß diesen Gleichungen allgem
kovariante entsprechen, falls der Skalar des Energietensors der

Thanks for this award and honor

And thanks to my wife Joan for her enduring support