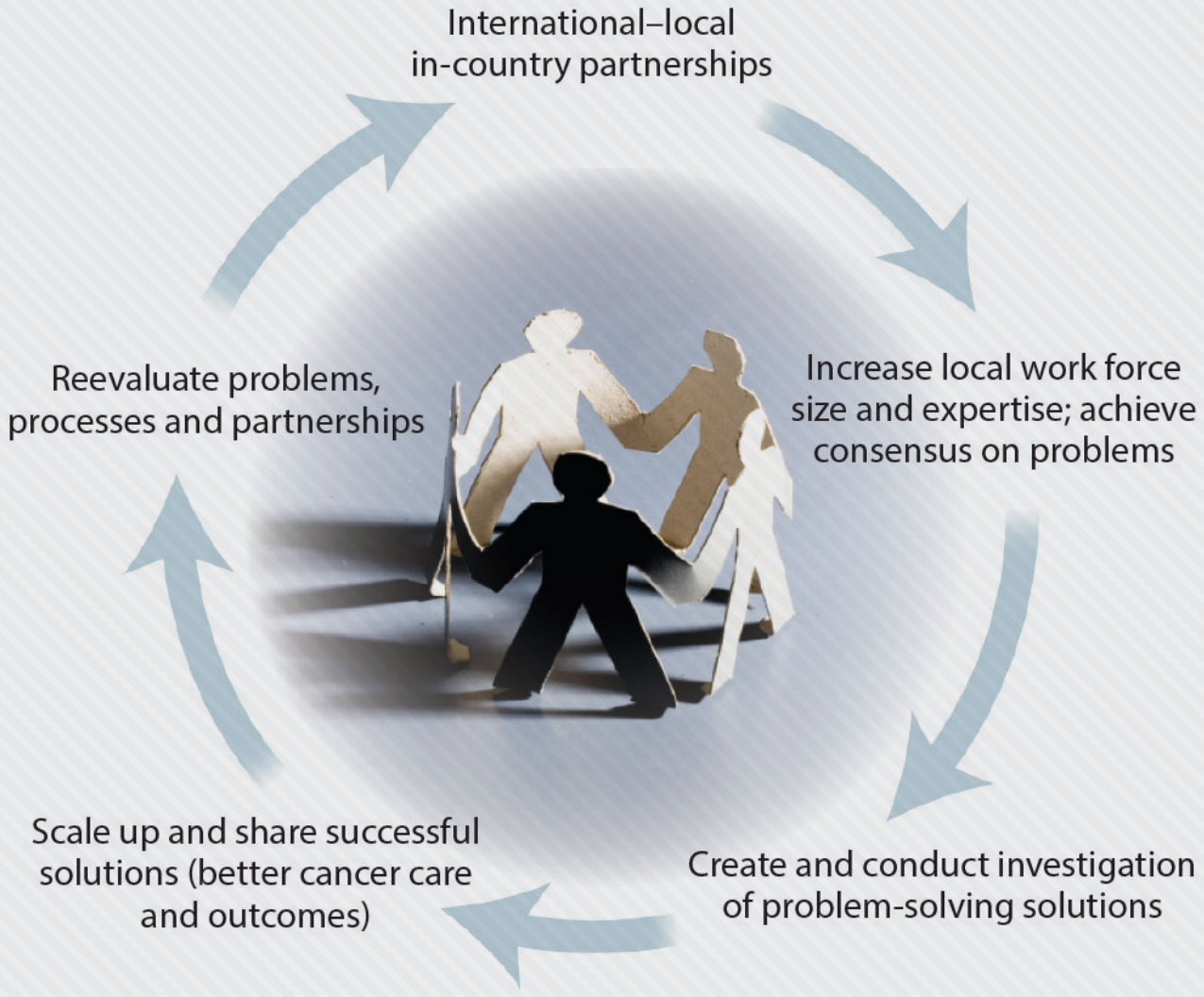
“SHADES OF GY”:

how can radiation be better used in cancer treatment

By C. Norman Coleman and David Pistenmaa (representing the efforts of many)

Think globally, mentor locally.



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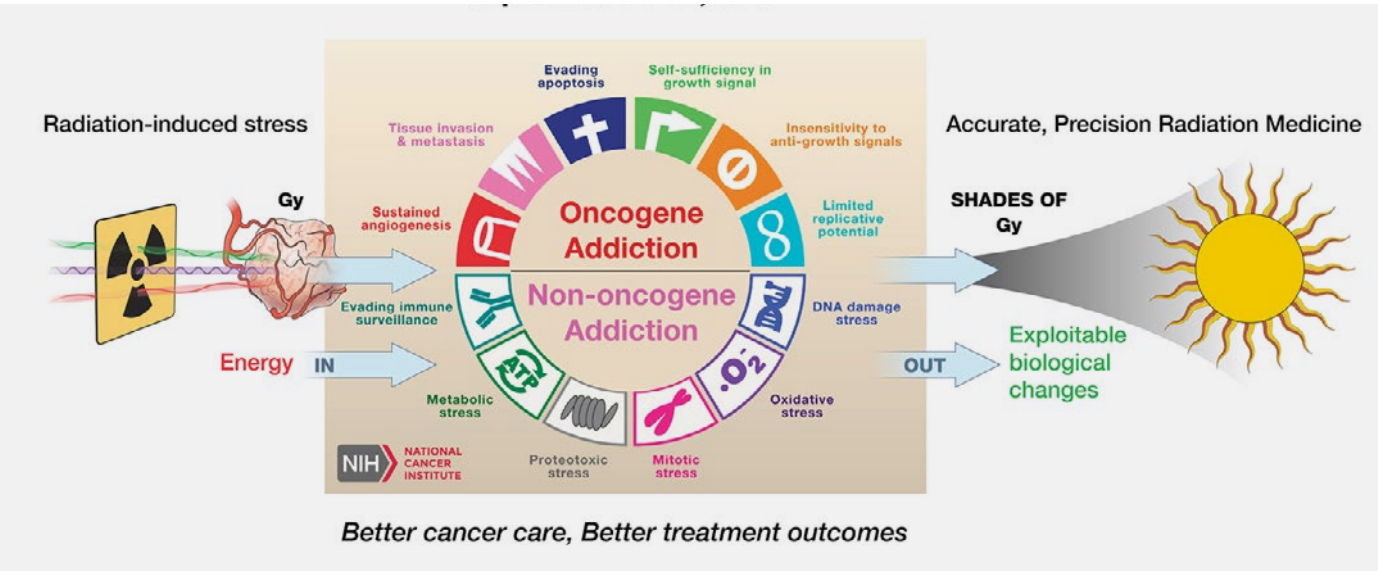


Figure 1

To best realise the breadth of potential contributions of the radiation sciences we tap into the expertise from CERN and the physics community. Their philosophy and experience with the establishment of effective global collaborations to address major challenges can help us identify new opportunities in the cancer field. In particular, we would like to address the "leading edge" of the radiation sciences in understanding how radiation interacts with tissue and the "trailing edge" in access to cancer treatment resources and how the innovation in linear accelerator design and the establishment of mentorship and educational programs can have global impact on the dire shortage in cancer care globally.

The **"leading edge" issue** was addressed in September 2017 at the US National Cancer Institute (NCI), "Shades of Gy" workshop. We know that, in order to understand the interaction between radiation and the biological tissue, the quantity of energy deposited in matter must be accurately described, measured and reported. The gray (Gy), (one joule of radiation energy deposited per kilogram of matter) is the unit of measurement. However, tissue, cells, and molecules do not "see" Gy but rather they absorb the energy and respond to it. At the workshop, several experts discussed the various aspects related to this issue and in particular: the dose-effect models (what do they tell us about biology and what do they allow us to do safely? Does comfort with them dissuade us from considering mechanisms and result in missed opportunities?); biophysics (why track structure from various forms of radiation and the various tissues, cells, organelles and molecules that are hit strongly suggest that simple RBE measurements will have limitations); the Relative Biological Effectiveness (RBE) and the range of endpoints used from organism down to molecular level and impact of biological perturbations as assessed in terms of dose size, dose rate and radiation quality; biomarkers and response predictors (how can one measure "radiation effect"?). The workshop was also an opportunity for clinicians to share their perspective on "dose" and desired outcome and to discuss the biological consequences of clinical relevance. Two more sessions were dedicated to discussions about whether we can consider partial tumour volume radiotherapy in the clinic that has the proposed potential to protect normal tissue & cells and elicit intra-tumoural & distal immune attack; and what conventional accepted wisdom of radiobiology that needs re-validation using modern tools for proper use in the clinic.

The final discussions focused on the famous the ratio (level of damage produced by one beam, for example X-rays, compared to the same level of damage produced by another beam for example a proton beam) used to determine the prescribed proton dose based on the experience with a defined photon dose. An RBE of 1.1 has been used for protons. However, at previous NCI workshops (reports to be published soon), it has been recognised that a simple ratio is not the optimal way to determine dose. The "Shades of Gy" was chosen for the title of the workshop because there needs to be a new major effort to determine dose in cancer treatment both by the energy absorbed and also by the biological changes induced by a specified dose. As discussed in the workshop, the consequences of radiation exposure, especially following adaptation of multi-fraction radiation therapy, has opened up potentially unique uses of radiation.

Figure 1 is the conceptual illustration of the innumerable physical and biological interactions of ionising radiations (reprinted with permission). A detailed publication will be forthcoming in the next year. What was clear at the workshop and subsequent meetings of American Society of Radiation Oncology (ASTRO) in September and the Radiation Research Society meeting in October is that the new "Shade of Gy" paradigm will be pursued as research and development in the radiation sciences broaden its scope to meet the opportunities, challenges and possibilities of having a substantial impact on improving human health. This applies to both the treatment of cancer and normal tissue injury.

The **"trailing edge" issue** was addressed at the CERN-ICEC-STFC Workshop held in October 26-27, 2017 at CERN.

International Cancer Expert Corps

Partnering to transform global cancer care

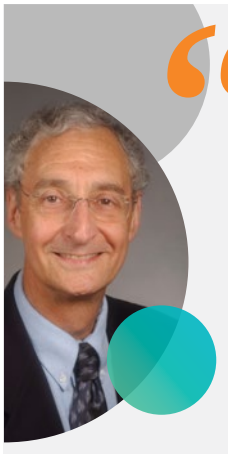
The International Cancer Expert Corps (www.iceccancer.org, ICEC) is a global organisation with members in Europe and Asia as well as in North America and is in the process of establishing offices in a number of countries. It has a dual effort to improve cancer care globally, including but by no means limited to radiation therapy, through 2 major efforts: a global mentoring and education network and improving the technology.

To follow up on the recommendations emanating from the first CERN-hosted workshop in November 2016, three task forces were created and began their work in 2017. The task forces are as follows:

- Task Force 1 – Technical ("Bury the complexity")
- Task Force 2 – Education, Training and Mentoring.
- Task Force 3 – Global Connectivity and Development

At an ICEC meeting during the International Conference on Advances in Radiation Oncology (ICARO2) in Vienna, in June 2017, it was agreed that a technology-only workshop should be the next step. Fortunately, the STFC (Science and Technology Facilities Council) agreed to co-sponsor with ICEC and CERN another workshop at CERN on October 26-27, 2017. The highlights of this meeting included presentations by radiation oncologists from Ghana, Tanzania, Zambia, Botswana describing the shortfalls in cancer care in those countries and their efforts to develop cancer care programs. A presentation by a physician from Jordan reported on the successful development of the King Hussein Cancer Center in Amman.

While outreach and development are necessary to implement mentoring programs, there are at least 20 existing potential ICEC mentoring programs that will build on ongoing established twinning relationships between experts in cancer centres in upper-income countries and associates in cancer facilities in developing nations. Interested parties are encouraged to register at the ICEC website (iceccancer.org). During the year between the workshops hosted by CERN in November 2016 and October 2017, ICEC has developed pathways for program building and recruitment. Particularly important for the enhancement of global health has been the commitment of "early career" individuals to the mission of improving cancer care globally. Thus, challenges at both the "leading" edge and the "trailing" edge of the radiation sciences and of oncology care are leading to unique programs, new partnerships and career opportunities with extraordinary potential to improve cancer care globally. ■



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