

incorporate an increasing amount of biological information of relevance to therapy response into planning and adaptation of the treatment of *individual* patients. Understanding and validating the clinical implications of biological information is a first critical step. Investigating whether non-invasive technologies may provide the pertinent information about these biological features is a second requirement if adaptation in the time-domain is to be achieved. Lastly, developing strategies that incorporate and weight the impact of a multitude of biological inputs is a third and unresolved scientific issue on which treatment adaptation rests. This includes a number of steps from the laboratory

to prospective clinical trials, for many of which medical physicists are key players. These components - on which the very concept of biologically guided adaptation of radiation therapy relies - must be critically addressed and the solutions and strategies validated before we can hope that the concept will enhance the therapeutic ratio on an individual patient level. The presentations at the BiGART2010 symposium showed that, although significant progress is evident, there is still a long way to go before individualised adaptive radiotherapy is a standard approach. A broad collection of the attempts to meet some of the unsolved challenges in this field have been compiled in a dedicated

BiGART2010 issue of *Acta Oncologica* (Vol 7, 2010, containing more than 40 papers) that will be available at the *Acta Oncologica* home page (<http://informahealthcare.com/onc>). ■

Dag Rune Olsen,  
Faculty of Mathematics and Natural  
Sciences, University of Bergen, Norway

In collaboration with  
Cai Grau, Jens Overgaard, Morten Høyer,  
Jacob Lindegaard & Ludvig Muren,  
Aarhus University Hospital,  
Aarhus, Denmark

## 3<sup>rd</sup> Modelling of Tumours (MOT) meeting

27-29 May, 2010 • Adelaide, Australia

It is a tribute to the energy and dedication of the organisers that a meeting on such a specialised topic succeeded in attracting close to 100 participants to one of the most geographically isolated cities in the world. The programme covered a wider spectrum of topics than its title suggests; my own talk on the first afternoon was one of the very few to deal strictly with the subject of "Tumour Modelling". The best way to summarise the proceedings is to pick out a few of the highlights.

Keynote speaker Andrzej Niemierko opened the meeting with the provocative title *Are we winning the "War on cancer"?* This was a comprehensive and often entertaining overview. We have now been treating cancer with radiation for an incredible 115 years. In 1971, the "war" began - President Nixon signed The National Cancer Act which made \$1.6 billion available to "make the conquest of cancer a national crusade". And since that "war" began, the US National Cancer Institute has spent \$105 billion. Despite this the death rates (per 100,000) from cancer were 157 in 1950 and 161 in 2000, whereas for heart disease the corresponding figures are

433 and 185. A telling statistic is that for localised disease the 5-year survival rates have shown modest improvements for prostate, breast and lung since the 80s but have remained totally flat for patients with distant metastases. Prof. Niemierko then moved on to the philosophy of modelling, stating that physicists and biologists often oversimplify clinical effects, and made us all laugh with "Alcohol & Calculus don't mix - never drink & derive." He demonstrated how important "scientifically sound radiobiological modelling" was to "treatment individualisation", illustrating this with the example of 2-year regional control for Head & Neck SCC increasing from 46% at 70 Gy to 61% at 80 Gy but making the point that for most patients that extra 10 Gy does nothing, except increase the toxicity risk. Further examples followed on how difficult it is to tease out a connection between toxicity and features of the dose distribution, due presumably to inter-patient variability of other factors. The near impossibility of mammography making a significant impact on breast cancer survival rates was also discussed. Finally a swipe at Big Pharma: "Why should the drug companies want to

cure us when they make more money from "treatments" for as long as we don't die?" We were urged to constantly question all dogma, with some more choice quotes.

Professor Roger Dale spoke on *High LET Therapy - the Radiobiological Challenge*. He began by making the point that the Relative Biological Effectiveness (RBE) of low-LET beams (i.e. the ones we use everyday) is the same everywhere; in a treatment plan we can simply add up doses from the different beams and thus evaluate the plan based on the total dose distribution. For high-LET beams this is no longer the case - the RBE may be spatially variant. The RBE for protons is around 1.1 and between 3 and 5 for carbon ions but the exact value depends on the beam energy, the dose level and the chosen biological endpoint. The telling point was made that we deliver conventional (megavoltage) radiotherapy with an accuracy in absorbed dose of 3% or better and therefore there is a need for the *radiobiological dosimetry* accuracy to be at least of the same order; merely assuming that the proton RBE is approximately 1.1 fails to do this. Prof. Dale suggested that the



Professor Dale meets a wallaby in Adelaide

that in the absence of transport via blood vessels, the range of signals is less than a millimetre over timescales of interest.

Roger Dale's second talk *Radiobiology and the Brachytherapy Renaissance* was a superb guided tour through the application of radiobiological concepts to brachytherapy, a subject which Professor Dale has contributed to hugely. He demonstrated beautifully the radiobiological commonality between external beam therapy and brachytherapy.

Professor Niemierko's second talk *Modelling Complex Phenomena* was firmly philosophical in nature. He questioned whether one could really apply the reductionist approach (i.e. that one can understand phenomena in terms of the properties of their constituent parts) to living organisms and in particular to cancer biology. Reductionism, whilst successful in physics, was next to useless in biology, and he illustrated this by reference to the Human Genome Project - only 300 of our genes are different from those of mice! Personally I wasn't quite sure what to make of all this. The phrase "All models are wrong, some are useful", from his first talk, came to mind.

And Adelaide itself? It is in the Top 10 in *The Economist's* World's Most Liveable Cities index. The centre is quite small, with the usual clusters of very tall buildings, but within walking distance there are many beautiful colonial style bungalows. It has 1.28 million inhabitants but the population density is very low with the city covering a vast area including a huge cricket stadium, vineyards, and a nature reserve up in the hills where Roger Dale and I observed at close quarters wallabies, pelicans, koala bears and other fascinating animals unique to Australia (see the picture!). Finally I should like to thank Professors Eva Bezak (Medical Physics) and Eric Yeoh (Radiation Oncology) and above all PA Christine Robinson for their quite outstanding hospitality. ■

Alan Nahum

operative quantity to use was not RBE but BED as this latter can take into account the total dose, number of fractions, the overall time,  $\alpha/\beta$  ratio, dose rate as well as the RBE itself - BED is the "radiobiological fulcrum of practical radiotherapy". Expressions for BED for both low- and high-LET radiations followed. As a postscript other therapy modalities were mentioned which also do not have unity RBE: low-energy emitters such as  $^{125}\text{I}$  (e.g. prostate seeds),  $\alpha$ -emitters, and low-energy x-rays ( $\approx 50$  kV) as used in the "Pappillon" technique - in none of these cases were the RBE effects usually taken into account. Professor Dale concluded with "Radiobiological modelling is growing up. It has an assured place in helping to guide the clinical use of high-LET radiotherapy."

After lunch I gave an overview of tumour control probability modelling, suggesting that this is in pretty good shape. We know how to incorporate dose, fractionation, tumour volume, radiosensitivity, non-uniform dose distributions, and also effects such as clonogen proliferation, overall time, and the prolonged delivery of a single fraction. The LQ formalism can also handle quite naturally the effects of

differences in dose not only from voxel to voxel but also from fraction to fraction in the same voxel, if this information is available (e.g. from image guidance). And as soon as we are in a position to replace population estimates of radiosensitivity and clonogen density by the values for individual patients (courtesy of the functional imaging of the future?), the model is ready to use these data.

Wendy Harriss (Adelaide) reported on a temporal Monte-Carlo tumour model simulating hypoxia in head and neck squamous cell carcinoma. She was able to explore the effects of reoxygenation and repopulation on the efficiency of tumour cell kill - definitely work to keep an eye on. Natalka Suchowerska (Sydney) discussed her group's puzzling *in vitro* finding that peripheral unirradiated cells can exhibit enhanced proliferation when lethal doses are administered to neighbouring (human cancer) cells - she calls this the *bystander type II* effect. Martin Ebert (Perth) then described his diffusion model of this cell-to-cell communication of radiation damage, which aims to elucidate whether these *in vitro* bystander effects really play a role in radiotherapy; his preliminary conclusions are