A brief history of radiobiology

Sometimes it is instructive (and interesting) to look back and see how far we’ve come, and what happened along the way. So here I have presented a short historical overview in graphical form together with some milestone papers.

A. GRAPHICAL OVERVIEW

Here are some of the major findings in radiobiological research since 1950. Because the vast majority of present research into radiation effects is at the molecular level, I have superimposed the history of some major milestones in molecular biology. This is not necessarily to say that looking at genes and molecular pathways is the only important thing to study. What happens at the cell, tissue and organism level is of course important, and ultimately what we are trying to explain. But we can’t do this without understanding what happens inside a cell, how it reacts to various stresses, how it interacts with its neighbours, how it reacts to various signals, what can go wrong, etc. Hence the superimposition of these two histories.

B. MILESTONE PAPERS IN RADIOBIOLOGY

In addition to the graph, I have listed below some of the most important papers which I think are milestones in the progression of understanding the effects of radiation on cells and tissues. I am sure there are papers I have left out, and some may be controversial and you may feel should not be included. If so, please tell me. Things are now moving very rapidly, and I am sure I have not done justice to all that’s happened and is happening in the present decade. So particularly here, suggestions are welcome.

ON PAGE 8, IN THE CLINICAL CORNER, YOU CAN READ ANOTHER REPORT OF THE WOLFSBERG MEETING.


1960's  


1970’s  

Douglas BG, Fowler JF. The effect of multiple small doses of X-rays on skin reactions in the mouse and a basic interpretation. Radiat Res. 1976 May;64(2):401-26


1980's  


1990's  


Ways to tackle hypoxia would include:
1) Increasing blood oxygen levels to reduce chronic hypoxic cells (get the oxygen to go further). Carbogen is an example being tested in the clinic.
2) Prevent the occurrence of acute (perfusion limited) hypoxia. Nicotinamide is an example being tested in the clinic (reduces vessel opening/closing, fast/slow perfusion).
3) Kill the hypoxic cells. Tirapazamine is an example of an hypoxic cytotoxin being tested in the clinic, although better drugs of this type are needed and being developed.
4) Sensitise the hypoxic cells to radiation. Nimorazole is an example, and used routinely with radiotherapy in Denmark. Some other methods are being tested pre-clinically.
5) Reduce the tolerance of hypoxic cells. This can be done for example with drugs affecting the unfolded protein response and the autophagy pathway. Such approaches and drugs are now being sought and tested.
6) Exploit hypoxia by administering anaerobic bacteria that will only grow in hypoxic/anoxic regions, and get these bugs to express something that kills or sensitises the hypoxic cells (and perhaps surroundingoxic cells).

Feedback

Thanks to Adel Coudri (Nice, France) who wrote the following concerning my answer to the question of the month in the last issue:

“Some readers might get confused about steepness and flatness. You wrote -Repeating a steep curve (high alpha/beta)…. Some people may think that a steep curve means high alpha/beta. Of course you know better than anyone that you may get a case with a high alpha/beta ratio, and a very small alpha, so that the dose-effect relationship is almost flat, not steep, yet linear. I think you should stick to what you wrote in the beginning of your answer, namely that a low alpha/beta means a curve with a high alpha/beta ratio, and a very small alpha, so that the dose-effect relationship is almost flat, not steep, yet linear. You may also add that when alpha/beta is high, the effect is almost proportional to the dose/fraction, whereas it is not in the case of low alpha/beta, because of the preponderance of the quadratic component, which is related to the square of the dose.” Correct of course…!

Thanks also to Daniel Taussky from Montreal for his positive comments.

Welcome to Physics in the Fall

The Autumn issue of Physics Corner includes a Classic Paper d.o.c., from 1946, on the radiological use of protons. Additionally there is a brief description of a very special technique based on the combination of a focused CT scanner beam with high density material to enhance dose deposition. At the moment it might have a limited spectrum of clinical application but this demanding paper is worth reflecting on, as it once more indicates how broad our work and research fields are. Our other short review concerns on-line treatment adaptation using “tomosynthesis” from the group of Karl Otto (of RapidArc fame).

ESTRO has many souls: one of them is Education. Brendan McClean, Director of Physics at St Luke’s Hospital in Dublin and Programme Director for the Irish National Training Programme for medical physicists, takes on board the very relevant question of who accredits education programmes in our field, starting from the Irish experience. His key message is that for European Medical Physics an accreditation body is very much needed.

Enjoy your reading and keep in touch with us!  

Giovanna, Ludvig, Alan

A Classic Medical Physics Paper

Radiological Use of Fast Protons
Robert J. Wilson, Research Laboratory of Physics, Harvard University, Cambridge, Massachusetts Radiology 47 487-91 1946.

Can it be true that as far back as 1946 a physicist was advocating the use of protons for radiation therapy? This paper is the proof of this remarkable fact. And we should remember that it wasn’t until 1991 and 1993 that the first patients were treated with a Cobalt 60 beam (in Canada and the USA) and by a linear accelerator (at the Hammersmith Hospital, London) respectively.

This paper is written in a style that recalls a bygone era. Its author, clearly a physicist, writes in order to communicate to a medical audience. He uses such straightforward English, with no attempt to “impress” anyone but nor is it at all condescending. I wonder if this has something to do with the fact that at the time there were hardly any “medical physicists” and thus no fellow scientists with whom to compete. I quote: “The object of this paper is to acquaint medical and biological workers with some of the physical properties and possibilities of such rays”. Beautiful!

We can also note that the author worked at Harvard University, which was subsequent-ly the place where proton therapy was developed and practised by some of the living legends in our field such as Michael Goitein and Herman Suit, and that today as we near the end of the first Decenium of the new Millenium, proton therapy is still not widely available and yet the arguments in favour of its use expressed in this paper were highly convincing as far back as 63 years ago.

The paper is so well written that one almost wants to reproduce every single sentence. Robert R. Wilson must have had a supremely gifted communicator. Try this for example: “The proton proceeds through tissue in very nearly a straight line, and the tissue is ionised at the expense of the energy of the proton until the proton is stopped…...The dosage is proportional to the ionization per centimetre of path….. and this varies almost inversely with the energy of the proton. Thus the … dose is