

Η βέλτιστη αλληλουχία
στην εποχή των πολλαπλών
θεραπευτικών επιλογών

15-16 Σεπτεμβρίου 2017

ΞΕΝΟΔΟΧΕΙΟ
Macedonia Palace
Θεσσαλονίκη



σενάρια συνδυασμού
ανοσοθεραπείας &
ακτινοθεραπείας

Ιωάννης Γεωργακόπουλος
Ακτινοθεραπευτής Ογκολόγος

δήλωση συμφερόντων

- I have no potential conflict of interest to report

ΓΕΝΙΚΑ ΣΤΟΙΧΕΙΑ

- RT: safe use of controlled doses of ionizing radiation to treat cancer
- as frontline therapy to approximately 60% of all patients with newly diagnosed cancer, usually in combinations with chemotherapy
- oligometastatic state
- palliative setting to address symptoms and enhance quality of life in patients with advanced tumors

ΓΕΝΙΚΑ ΣΤΟΙΧΕΙΑ

- understanding radiobiology: optimization of dosage and fractionation
- cutting edge technology:
 - intensity modulated radiation therapy (IMRT)
 - image guided radiation therapy (IGRT)
 - stereotactic radiosurgery (SRS)
 - medical imaging (π.χ. PET/CT)



precise delivery of higher doses of RT per fraction
(hypofractionation) with minimal damage to healthy tissues

γενικά στοιχεία

- ability to induce DNA damage with direct tumor cell death
- radiation induces cancer cell **extrinsic mechanisms** of tumor control
 - local control
 - control of metastases outside of the treatment site

ΓΕΝΙΚΑ ΣΤΟ

VOL. XXVI, No. 305

WHOLE BODY

Medical Research Council

cells or proliferating or actively meta-
are more radiosensitive than other cells.
This last principle has important exceptions
ever it is phrased. It is sufficient here to
repair of radiation damage takes place in bone
marrow or lymph nodes, then it cannot be true that
the primitive and undifferentiated cells are more
radiosensitive than those more mature cells which are
killed (see footnote on page 238).

The idea that the nucleus is the most sensitive
part of the cell was a deduction from the belief that
the nucleus controls cell growth and division, from
the visible changes the nucleus undergoes when the
cell is irradiated, and from the evidence that chromo-
some and genic damage are produced by radiation.
Trowell (1952) has pointed out that it is not legiti-
mate to conclude from the fact that structural
changes occur in the nucleus before the cytoplasm
that the nucleus is, in fact, damaged primarily and
not as a consequence of cytoplasmic damage.
Experimental evidence is not available for mammals,
and for other forms of life is conflicting (Vintem-
berger, 1928, 1929; Duryee, 1949; Harriss, Lamerton,
Ord and Danielli, 1952).

One result of belief in primary nuclear damage is
the idea that radiation induced changes in due to a

abscopal* effect

mean the effect on an object or irradiation of its
environment, and that some other word, for which I
have suggested abscopal, should be chosen for the
different sense of action "at a distance from the
irradiated volume but within the same organism".

This is not merely a theoretical discussion but
directly relevant to all work done on the effects of
whole body irradiation. One clear-cut example will
illustrate this. Three days after 600-1000 r, rats
show a depression to one-quarter of normal of the
synthetic ability of the thyroid gland (Mole and Batt,
1953). This is not due to whole body irradiation,
however, nor to direct irradiation of the thyroid or
the pituitary gland. The depression of thyroid
function appears only when a sufficiently large
volume of the abdomen is irradiated (unpublished
observations), and is therefore an abscopal effect of
radiation.

The effects of whole body irradiation are some-
times summed up as due to the cellular damage
radiation does. From one point of view this is a
valid way of stating the case, but it is not a
synonym for a certain amount of intercellular

duced?
that the
only be
ed it, to

MEDICINE?*

ment, Harwell, Berks.

* Ab- is a prefix with the meaning "position away from"
(*O.E.D.*) and scopos (Latin) is a mark or target for shooting
at. The derived adjective therefore conveys the exact mean-
ing required.

biological characteristic of organisms like mammals is
that it is literally impossible to produce an effect in
them limited to a small volume. The interdependence
of all the cells in the organism's body means that
damage to one cell must inevitably alter the body as a
whole, *i.e.* all the other cells of the body. This is
almost a biological platitude but it has such far-
reaching consequences that it needs stressing. For
example, it is meaningless to ask the question about
the mammal: Is there an indirect effect of radiation?
in the sense in which this question is normally
asked. It would be a sensible, if not very important
question if it meant: Does irradiation of the mam-
mal's environment have an effect? But normally
what the questioner means to ask is: Has irradiation
of a mammal an effect at a distance from the volume
irradiated? and to this there can only be one answer.
What is important is to ask: How much of this

biological characteristic of organisms like mammals is
self-evident, yet the rate of loss of cells from the per-
ipheral blood after whole body irradiation has been
used as a measure of their natural life span. For red
cells there is clear proof that the cellular hypothesis
is untrue. Haemorrhage and erythrophagocytosis
produce a loss of red cells which is not explained by
death of red cell precursors, and quantitatively even
more important may be the finding of widespread
capillary leakage of red cells (Furth, 1952). And if
the hypothesis is untrue for red cells why assume
that it is true for white cells or platelets? Every time
someone is taken off work with irradiation because
of a low white count, the assumption is made that the

* Ab- is a prefix with the meaning "position away from"
(*O.E.D.*) and scopos (Latin) is a mark or target for shooting
at. The derived adjective therefore conveys the exact mean-
ing required.

abscopal effect

immune dependent mechanisms

evident that this effect is mediated by immune mechanisms

- tumor specific
- does not occur in immunodeficient individuals
- could be potentiated by interventions that mobilized antigen presenting cells (APCs)

abscopal effect

- renal cell carcinoma
- malignant melanoma
- hepatocellular carcinoma
- lung cancer
- other tumor types & hematologic malignancies

immunobiology of RT

- ✓ RT induces in situ vaccination
- ✓ RT reprograms tumor microenvironment

in situ vaccination

