One Size Fits All: Does the Dogma Stand in Radiation Oncology?
David Azria, Céline Bourgier, Muriel Brengues

To cite this version:
David Azria, Céline Bourgier, Muriel Brengues. One Size Fits All: Does the Dogma Stand in Radiation Oncology?. EBioMedicine, Elsevier, 2016, 10, pp.19-20. 10.1016/j.ebiom.2016.07.025. hal-02294317
Commentary

One Size Fits All: Does the Dogma Stand in Radiation Oncology?

David Azria a,b,*, Celine Bourgier a,b, Muriel Brenquès b

a Department of Radiation Oncology, Montpellier Cancer Institute (ICM), Montpellier Cancer Research Institute (IRCM), University of Montpellier, Montpellier, France
b INSERM U1194, Montpellier Cancer Research Institute (IRCM), University of Montpellier, Montpellier, France

Article history:
Received 18 July 2016
Accepted 18 July 2016
Available online 20 July 2016

External beam radiotherapy (EBRT) is the most treatment used in solid tumors as nearly 50% of cancer patients receive curative EBRT in the world. Its success depends mainly on the total dose homogeneously delivered within the target volume. Nevertheless, EBRT inevitably exposes normal tissues and may cause late and sometimes irreversible toxicities depending on different cells or tissues (stroma, vascular, parenchymal, immune cells). Interactions between cells or compartmental tissues and the immune system via cytokines produce inflammatory and pro-fibrotic reactions. Cell depletion, inflammation, repopulation and remodeling are reminiscent of the wound healing process leading to different severities of late deterministic effects (Herskind et al., 2016).

Stratifying patients according to the toxicity risk and modulating EBRT dose would provide a valuable tool for personalized EBRT (Barnett et al., 2009; Bourgier et al., 2015). Many efforts have been made to develop assays capable of predicting susceptibility for the development of radiation injury that finally allow customization of EBRT protocols on an individual basis.

Indeed and as presented in this current volume of EBioMedicine, Kerns and colleagues (Kerns et al., 2016), aimed to meta-analyze individual level data from four genome-wide association studies from prostate cancer radiotherapy cohorts including 1564 men to identify novel genetic markers of toxicity. A fixed-effects meta-analysis identified two SNPs: rs17599026 on 5q31.2 with urinary frequency and rs7720298 on 5p15.2 with decreased urine stream. These SNPs lie within genes that are expressed in tissues adversely affected by pelvic radiotherapy including bladder, kidney, rectum and small intestine. The authors mentioned that new moderate-penetrance genetic variants as-
(Azria et al., 2008); (ii) Protein and ROS production modification, enhanced genomic instability, terminal differentiation of fibroblasts and increased risk of fibrogenesis (Lacombe et al., 2013); (iii) genetic defect in the DNA damage response, DNA repair reduction, increased genomic instability and increased premature terminal differentiation of fibroblasts (Herskind et al., 2016).

Clinical implementations with interventional protocols are starting using this assay permitting distinction between patients without any over-risk of toxicity (considered as resistant to late effects) and patients clearly at risk of developing more late effects defined as very sensitive (Barnett et al., 2015). In terms of altered management, hyperfractionation can reduce toxicity with no risk of loss of local control or to allow for dose escalation in very sensitive patients. For more resistant patients, an increase in dose should be possible and hypofractionation regimen should be largely proposed leading to a medicoeconomical improvement of our treatments. This might be in favor of adding novel targeted or existing systemic therapies (Barnett et al., 2015).

In conclusion, there is no doubt that personalized radiotherapy driven by companion tests of radiotoxicity but also of tumor radioresponse will be the standard of care in the near future as it is already the case for targeted therapies in medical oncology. One size will no longer fit all!

Disclosure

The authors declare that they have no competing interest regarding this manuscript.

References


