Particule versus photon radiotherapy (RT) impact on toxicity in children: Which evidences?

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Objective: Evaluating the place of particle therapy (mainly protons) in children/adolescents, from an extensive literature review in terms of acute/long-term toxicity, and with focus on inter-comparative studies.

Methods: We performed a review of published articles, from 1997 through 2018, based on Medline, according to the following keywords: English, toxicity, novel technologies. Dosimetric (dos) investigations, secondary cancers (K2) predictive models, and clinical series were evaluated separately. Our project was focused on published inter-comparisons between particles (P') and photon-therapy (XR), either 3D or intensity-modulated (IMXRT), with their degree of significance: "ps" if >0.05 in all publications (pub), "mixed" ps and non-ps pub, or "NS" (not significant) in all analysed pub. 162 pub were retrieved, from which 27 pre-clinical, and 13 clinical were eligible.

Results: They are displayed from tables 1 to 3, for the three categories mentioned above.

Discussion: P provided a universal benefit over XR for most endpoints, analysed in dos and model studies, but was more contrasted in clinical ones:

-Dosimetry studies: P-XR was observed in all evaluated organs or functions, concerning CNS and extra CNS primaries. Among 11 CNS endpoints, only one was NS (cognition in supratentorial tumours), and 2 "mixed" (brain + cognition in CS RT). Among 5 MN endpoints, all were ps. Among 8 endpoints in the trunk, 8 were ps, and one NA.

-Model-based K2 studies: P-XR was reported in 1/10 evaluated organs exposed to K2 (pancreatic K2), and P-XR in 9/10, but with only 2 ps ("body") i.e. Integral dose for MN and abdomino-pelvic tumours. In CS RT, "mixed" degrees of significance concerned most anatomical structures anterior to the spine.

-Clinical studies: Among the cohort of 1,740 patients (approximately half P, and half XR), analysed for 6 toxic endpoints, P-XR was reported in 2/3 acute, and 2/3 cerebral side-effects, including cognition, with the noticeable exception of schooling performances. But it is noteworthy that P-XR was reported in brain radionecrosis, salivary, and pulmonary toxicities, with high ps value.

Conclusion: The vast majority of published series dealing with dosimetry and K2 modeling were in favor of particle therapy to limit radiation toxicity, although p< value was not systematically quoted. Similar trend concerned clinical evaluations, but the data remained scarce, never randomized, and mainly related with CNS. If particle therapy is becoming popular, it remains essentially based on dosimetical CNS investigations, and further clinical evidences are warranted. The pancreatic, pulmonary and salivary impact, as well as schooling performances should be revisited, at the light of new studies.