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The "old" or "new" spinal cord? Problems of tolerance in postirradiation myelopathy

Krzysztof Składowski

I Radiotherapy Clinic, Oncology Institute, ul. Wyb. Armii Krajowej 15, 44-101 Gliwice

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The last few years have seen a number of interesting research reports on the biology and pathogenesis of post-irradiation effects in the spinal cord [1-3].They all seem to indicate that myelopathy is caused by structural damage to neurologic cells and blood vessel endothelium preceded by a humoral inflammatory reaction which starts directly after irradiation. Repair mechanisms, mainly those concerning the glial cell proliferation process which begins several to several dozen weeks after the irradiation, have also been described. It is also known that at least 12 months after radiotherapy the spinal cord "forgets" about half of the dose administered [4].

The report "Radiation myelopathy: a radiobiological review" by A. S. Shirazi, S. R. Mahdavi and K. R. Trott in the present issue of *Reports of Practical Oncology and Radiotherapy,* is an overview dedicated to these problems [5]. What is more, it provides a simple and lucid description of the methods and research techniques used in laboratory studies. In my opinion, the most valuable element of this work is the chapter presenting the linear-quadratic model of radiosensitivity of the spinal cord. In its conclusions it is stated that for the irradiation with fractionated doses between 2 and 19 Gy the α/β ratio is roughly 2.5 Gy, whereas for the dose range of 1-2 Gy this coefficient was found to be 0.48 Gy, i.e. lower by a factor of 5, which is reflected by a much higher increase in radiosensitivity of spinal cord. Therefore, the authors conclude that for irradiation with doses lower than 2 Gy, the use of α/β coefficient of 2-2.5 Gy in the model of equivalent doses (NTD), may results in the underestimation of the tolerance dose (TD) for the spinal cord.

The above conclusion seem to call for some comments. The question of a tolerance dose for the spinal cord in oncological radiotherapy has been raised on and off in medical literature for several dozen years. Now, when conformal radiotherapy, simultaneous chemotherapy and non-conventional methods of dose fractionation have been universally adopted, this problem has acquired particular importance. This is all the more true in the situation where radiological presumptions (also exposed in the paper under discussion) have made us more inclined to debunk or neglect the long-established thesis that the tolerance dose for the spnal cord should be adopted at about 45 Gy administered in conventional 2 Gy fractions.

As early as 10 years ago some leading Polish specialists in radiotherapy held a discussion on this subject in the journal "Nowotwory" (Neoplasms) [6]. It was then believed that it would be too dangerous to exceed the above dose to the spinal cord in routine irradiation practice, and although even then quite a number of reports indicated that this dose should be elevated by 5-10 Gy, this statement was explained by several factors such as the gravity and lack of success in the therapy of complications, lack of routine irradiation quality control procedures, particularly intravital dosimetry and lack of identification of higher other extra-radiational risk factors of mlyelopathy.

Since then the views on the tolerance of spinal cord irradiation have not changed. What has changed, however, is radiotherapy as such mostly due to great technological development. At present, the spinal cord is found in almost all virtual radiotherapy planning procedures, most often in the form of an outline of critical organs, for which the therapy plan envisages specific radiation doses and depicts them as histograms of irradiated volumes. Here, in my opinion, "is the rub": which of the dose histograms should be adopted for the spinal cord, in other words, which one should be considered optimal in view of its tolerance for the patients safety? The answer to the question simple as it may seem is not easy, except in the case of conventional fractionation procedures when the full histogram lies below the tolerance dose of 45 Gy and thus can be accepted unreservedly. The situation that is most often encountered is that the dose histogram shows that the value of 45 Gy is exceeded in some portion of the irradiated volume. In this case the safest solution seems to be making a statistical analysis of the dose distribution. The radiotherapy plan may by accepted when the mean values such as the arithmetic, medial and modal means do not exceed the tolerance dose, whereas the minimum and maximum doses for 5% cord volume (the right end of the histogram) will not exceed 50 and 55 Gy, respectively. It also seems that all the above doses should be decreased of 10% when chemotherapy is applied, especially when anticancer agents such as cisplatine metotrexat or etoposit [7] are administered in combination with irradiation.

A rather different approach is called for when we want to estimate the spinal cord tolerance doses in non-conven-

tional irradiation fractioning procedures. The application of 2-3 dose daily with short (4-6 h) interwal above the mentioned tolerance dose may lead to an elevated level risk of myelopathy 3[8]. Therefore, when using hyperfractionation or accelerated fractionation one should ensure that the intervals between doses should be at least 6-8 hrs and the tolerance dose should be lowered by 10-15%.

Conformal radiotherapy, especially its form implemented with the use of dose intensity modulation (IMRT), in many cases makes it possible to almost totally exclude some organs from the irradiated volume, including the spinal cord. This technique seems to be best suited in the situation when we have no other choice but to decide to a second course of irradiation of a patient with recurrent cancer. We should, however, remember to ensure maximum protection of the spinal cord not only in rare cases of retreatment, but also in everyday clinical practice.

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