LOW OR HIGH FRACTIONATION DOSE B-RADIOTHERAPY FOR PTERYGIUM? A RANDOMIZED CLINICAL TRIAL: IN REGARD TO VIANI GA *ET AL.* (*INT J RADIAT ONCOL BIOL PHYS* 2010;10.1016/J.IJROBP.2010.11.017)

To the Editor: We read with interest the randomized clinical trial that compared low- versus high-dose fractionation β-radiotherapy for pterygium (1).

This is the largest prospective randomized trial that addressed the value of beta irradiation after surgical excision of pterygium after that of Jurgenliemk, 86 cases (2), Nakamatsu , 73 cases (3), and De Keizer, 57 cases (4). It is also the first one that compared low-dose fractionation (20 Gy/10 fractions) with higher dose per fraction regimens (35 Gy/7 fractions).

The rate of pterygium control was 93.9% with 20 Gray/10 fractions arm versus 92.3% with the 35 Gray/7 fractions arm which was not far from local control rates reported by Jurgenliemk (2) with single dose of 25 Gray (93.2%) and the 90% local control rate reported by De Keizer (4) using 27–30 Gray/3 fractions.

In view of the significant difference between both arms in the incidence of photophobia, irritation, postoperative granuloma, cosmoses, and scleromalacia in favor of the low dose per fraction regimen along with the no difference in the pterygium control rate, the authors recommended the use of low dose per fraction regimen rather than the hypofractionated ones.

This may be understandable in the light of radiobiological work conducted by Brenner and Merriam (5), who estimated large value of α/β ratio of nonrecurrence that suggests improved therapeutic ratio from fractionated application of β irradiation. But practically speaking, application of high dose per fraction regimens with doses from 30–60 Gray in three to six fractions or even a single high dose (2, 6, 7) was not reported to be associated with high incidence of late complications (*e.g.*, scleromalacia, sclera ulcers, corneal ulcerations, necrotizing scleritis, maculopathy) that could occur even with surgery alone without radiotherapy (2, 8, 9).

In the light of the above mentioned discussion, and the many studies that used high dose per fraction regimens reported in our review article (10), we recommend the use of the hypofractionated regimens from the prospective of better patient compliance, especially in centers with limited resources and personnel.

Ali Mohamed Ali, M.D.
Department of Clinical Oncology
Sohag Faculty of Medicine
Sohag East, Sohag, Egypt

Juliette Thariat, M.D.
Department of Radiation Oncology
Center Antoine Lacassagne
University Sophia Antipolis
Nice, France

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IN REPLY TO DRS. MOHAMED AND THARIAT

To the Editor: Our article compared a higher biological effective dose (BED) schedule (7×5 Gy) versus a lower BED schedule (10×2 Gy). Our results showed a similar pterygium control and more adverse effects in higher BED arm (1). This result raises two questions on radiotherapy treatment for pterygium: First, what is the real value of alpha/beta for pterygium? And second, why were our results different from that in the literature? Several studies have estimated the alpha/beta for pterygium from a wide variety of doses and fractionation schemes used in clinical practice. However, few studies have used doses and fractionation schedules with lower BED.

Three studies on this issue have concluded that higher BED (>30 Gy) is better than lower BED to prevent recurrences (<10%) (2–4). But in these analyses only two studies had a BED lower than 30 Gy (5, 6). Therefore, how can we conclude that higher BED is better than lower BED?

The only randomized study evaluating different doses for pterygium (7) compared 30 Gy/three fractions (high BED) with 40 Gy/four fractions (high BED) achieving 85% versus 75% of pterygium control at 2 years, respectively.

Based on a higher BED concept, it would be expected that BED >30 Gy resulted in lower (<10%) recurrence rate in the both arms. Why didn't this happen?

For us, the difficulty in understanding these differences show the weakness behind the calculation of pterygium BED. Because the pterygium alpha/beta was calculated combining results of different studies with a lot of bias (retrospective design, lack of information, different time of follow-up, fresh and recurrent pterygium, and small sample). Consequently, we can be over- or underestimating the results. All studies cited previously include retrospective studies, all with bias (2–4). Furthermore, if we consider the pterygium BED as high as 25 or more, this probably indicates that the pterygium is a highly sensitive tissue to radiation, and being a sensitive tissue, we will not need a high BED to achieve satisfactory local control. For example if the alpha/beta pterygium was 100, the BED for 10×2 Gy and 7×5 Gy would be 20.4 Gy100 and 36.7 Gy100. In other words, the pterygium control wouldn't depend so much of the total dose. Looking at the results from this point of view, we can understand more easily the results found in our trial.

Gustavo Arruda Viani, M.D.
Ellen Carrara Fonseca, M.D.
Department of Ophthalmology
Marilia Medical School, Marília
São Paulo, Brazil

Ligia Issa De Fendi, M.D.
Department of Radiation Oncology
Marilia Medical School, Marília
São Paulo, Brazil

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