Re: Bressler et al.: Factors associated with worsening proliferative diabetic retinopathy in eyes treated with panretinal photocoagulation or ranibizumab. (Ophthalmology. 2017;124:431-439)

TO THE EDITOR: We read the article by Bressler et al1 with great interest and would like to share our concerns about the panretinal photocoagulation (PRP) treatment performed in the original investigation “Panretinal Photocoagulation vs Intravitreous Ranibizumab for Proliferative Diabetic Retinopathy.”2 To assess the efficacy of PRP, one must evaluate the total area of retina treated, as indicated by the laser spot size, pulse duration, lesion intensity, and number of laser burns. Analysis of the DRCR Protocol S trial2 suggests that many patients in the study, particularly those receiving pattern scan (PASCAL) laser, received incomplete PRP.

The PASCAL laser creates patterns of multiple spots using a scanning laser that requires a shorter pulse duration, typically 20 ms.3 Even with the same moderate intensity PRP burns, shorter pulse duration PASCAL spots are smaller in size and thus require more spots for a similar treatment efficacy.3 To match the same total treatment area compared with conventional laser burns, the number of PASCAL laser burns must increase as the reciprocal of the square of the lesion diameter. For example, for a 200-μm spot size, 1000 conventional laser burns are equivalent to 5017 barely visible PASCAL burns, 2783 light PASCAL burns, and 1932 moderate PASCAL burns.5

In the DRCR Protocol S study, the PRP group treatment guidelines were moderate laser burns defined as “1200–1600 burns using conventional laser or 1800–2400 burns using an automated pattern delivery system, completed in 1–3 visits.”2 For conventional laser, a mean of 1440 spots (range, 1274–1600) were applied with parameters of 500-μm spot size and 100-ms pulse duration of mild white (2+ to 3+) intensity (see Table S3 in the original article, available at www.aaojournal.org).2 For the PASCAL laser, a mean of 2190 spots (range, 1831–2416) were applied with parameters of 400-μm spot size, 20-ms pulse duration of mild white intensity.2

The treated retinal area can be expressed mathematically as:

\[ A = \frac{N \times \pi \times (D \times Mag \times g)^2}{4} \]

where \( A \) is the treatment area; \( N \), number of laser spots; \( D \), aerial beam diameter; \( Mag \), lens magnification (e.g., 1.05 for Ocular Instruments Mainster Standard Lens and 2.00 for Volk SuperQuad 160); and \( g \), coefficient that is a function of lesion grade, pulse duration, and retinal beam size. For moderate intensity burns with a 400-μm aerial spot size, \( g \) is 1.39 for 100-ms conventional burns and 1.15 for 20-ms PASCAL burns.3 To achieve a treatment area equivalent to the area treated with the mean number of 1440 moderate intensity conventional 500-μm spots, a total of 3287 PASCAL spots with 400-μm size should be applied, as calculated with the following equation:

\[ \frac{1440 \times \pi \times (500 \times Mag \times 1.39)^2}{4} \]

\[ = \frac{N \times \pi \times (400 \times Mag \times 1.15)^2}{4} \]

In this study, PASCAL-treated patients received a mean of 2190 spots laser spots, which is significantly less than that received by patients treated with conventional laser (equivalent of 3287 spots). This substantial under-treatment likely explains the authors’ observation that in the Protocol S study, the PASCAL laser led to worse outcomes.1

In addition, Table 1 in the original article indicates that 44% of eyes received <1400 conventional laser spots or <2200 PASCAL spots and thus received less complete PRP. Univariate analysis reveals that of those eyes with less complete PRP treatment (<1400 conventional laser spots or <2200 PASCAL spots), 53% had an event compared with only 37% of eyes receiving more complete PRP. The 37% event rate seen in eyes receiving more complete PRP is comparable with the 34% event rate seen in eyes receiving ranibizumab. Thus, it is not PRP per se, but rather incomplete PRP that is a risk factor for worsening proliferative diabetic retinopathy as defined by the authors.

This analysis should emphasize to retina specialists that adequate PRP is critical to the effective treatment of proliferative diabetic retinopathy. In addition, it is important when using the PASCAL laser to deliver significantly more laser spots to treat a retinal area equivalent to that treated with conventional laser PRP. Finally, we have reservations about using DRCR Protocol S results to draw firm conclusions about the relative benefits of ranibizumab versus PRP in eyes with proliferative diabetic retinopathy, given the undertreatment with PRP delivered in the study.

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References


