

## **Cochrane Corner: wavefront-guided laser vision correction**

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Li et al.<sup>1</sup>, are the latest group to evaluate results for wavefront-guided and wavefront-optimised laser vision correction (LVC) in a systematic review. Using Cochrane methodology, they found no significant differences in pooled visual results from 33 randomized trials including 1499 patients. But does this mean that clinically important differences do not exist?

The jargon is confusing. Higher order aberrations are elements of defocus that remain after correction of sphere and cylinder. Zernicke decomposition is used for classification and ranking. In this system, 3rd and 4th order aberrations (coma, trefoil, and spherical aberration) and the total score, expressed as a root mean square function, are the most widely studied clinical indices. Aberration scores are commonly expressed in microns for the eye measured and depend on pupil size at the time of measurement. Using a simple conversion formula described by Thibos et al.<sup>2</sup>, they can also be expressed as equivalent dioptric values, and this helps add clinical meaning.

The first task in LVC is to correct for aberrations induced by treatment. This is what “wavefront-optimised” or, more correctly, “wavefront-compensated” (WFC) LVC treatments seek to do. WFC treatments build in corrections based on mean changes in higher order aberration terms observed in a patient sample treated with a given magnitude of sphere and cylindrical correction. All modern LVC systems incorporate some form of wavefront-compensation; but newer systems using larger optical zones, smoother ablation profiles, more accurate treatment registration, and faster eye-tracking are more effective.

Wavefront-guided (WFG) treatments layer-on an additional element of individual customisation by targeting higher order aberrations measured preoperatively. Since these total around  $0.25D^2$  in normal eyes, any gains from wavefront-guidance in routine LVC treatment are likely to be small. But WFG treatment may also help to enhance accuracy of sphere and cylinder outcomes.

In their first analysis, Li et al.<sup>1</sup> have categorized some older laser systems, with more basic wavefront-compensation, as “conventional treatments,” comparing results with newer WFC or WFG excimer laser platforms. Results are largely historic, with the last trial included reporting in 2012; and results are likely to have been skewed against the newer laser systems by relative immaturity of nomogram development. Other systematic reviewers have detected a trend towards better results for newer LVC technology<sup>3</sup>, and this trend is also evident, although not picked up, in better visual results for the later trials analysed by Li et al.

Systematic reviews of randomized trials are less easy to interpret for technologies in evolution than for drug treatments. Both WFC and WFG excimer laser platforms have evolved significantly in the time period (late 1990s–2019) Li et al. study<sup>1</sup>. Most of the trials they include in their comparison of WFG and WFC treatments compare an older WFG excimer laser platform (CustomVue Star S4 IR excimer laser; Johnson & Johnson Vision, Inc., Santa Ana, California) with a newer WFC platform (Wavelight Allegretto Eye-Q 400 excimer laser; Alcon Laboratories, Inc., Fort Worth, Texas) incorporating significantly faster ablation and a larger optical zone size. If wavefront compensation is more effective for the newer laser, any gains from wavefront-guidance will have been masked. To determine whether WFG treatment

improves visual results, both the mechanism of wavefront compensation and the maturity of nomogram development need to be standardised between trial arms. Otherwise, you are, in effect, comparing apples and pears.

Li et al finish with a comparison of WFG LASIK versus WFG PRK. Similar comparisons have already been widely covered<sup>4,5</sup>. Like Li et al, previous systematic reviews have concluded that any differences in safety or efficacy between the main LVC modalities (LASIK, PRK and SMILE) are small—they all produce good results.

Many LVC studies fail to include patient reported outcome measures (PROMs). PROMs are particularly important in studies of WFG treatment, since wavefront-guidance seeks to improve satisfaction with visual quality over and above any effect on refraction outcomes and visual acuity. Standard reporting for refraction outcomes<sup>6</sup> is now widely disseminated, but there is still no consensus on which PROMs clinical trials in refractive surgery should incorporate. This reflects deficiencies in the PROMs that current refractive surgery investigators have at their disposal.

Around 98% of patients are satisfied with the outcome of contemporary LASIK, the most widely used LVC modality<sup>3</sup>. Against this high bar, advances in LVC are defined by continued marginal gains. The danger in a superficial reading of this and other systematic reviews of LVC techniques is that the headline finding, no statistically significant differences between platforms at a snapshot in time, will discourage exploration and uptake of new technology. It also fundamentally misinterprets what Li et al are saying. A key goal for Cochrane Reviews is to highlight deficiencies in the existing evidence base. Li et al are clear throughout that their failure to find

significant clinical effects may simply reflect methodological problems with the randomized clinical trials they reviewed.

Despite flaws in the existing evidence base, other systematic reviewers looking at the impact of WFG treatment have found advantages for astigmatism<sup>7</sup>, and for postoperative higher order aberration scores in patients with higher preoperative levels<sup>8</sup>.

Outside the narrow lens of randomized trials, there are strong, a priori arguments for using WFG treatment<sup>9</sup>. Measurement repeatability (precision) is around twice as good as manifest refraction for modern Hartmann-Shack and pyramidal aberrometers. Surgeons are also protected from making transcription errors in treatment programming by direct import of key treatment indices into treatment programming software.

Wavefront compensation is always desirable. But does wavefront-guidance produce genuine marginal gains in routine LVC? To answer this question, we need better PROMs and comparisons between excimer laser systems with both matched wavefront compensation and mature nomogram development. At minimum, WFG systems developed for routine LVC have widened the range of therapeutic excimer laser treatments we can now safely perform.

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