

Elsevier Editorial System(tm) for Journal of Cataract & Refractive Surgery  
Manuscript Draft

Manuscript Number:

Title: Keratoconus exacerbation after cross-linking and surface ablation - a case report

Article Type: Case Report

Section/Category: Refractive

Keywords: cross-linking; keratoconus; PRK; keratoconus progression

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**Abstract:** Purpose: Topography-guided photorefractive keratectomy (PRK) in cases of forme fruste keratoconus is considered a treatment option for optical rehabilitation. Recently this approach was proposed for keratoconus corneas after corneal cross-linking (CXL). We report a case where the photoablation reinitiated progression of keratoconus.

**Patient and methods:** A patient with bilateral keratoconus underwent bilateral CXL with a stabilization of corneal topography after treatment. Customized PRK (topography-guided) was performed in the left eye at 2 years after CXL.

**Results:** Immediately after PRK the eye showed progression of the keratoconus, whereas the right eye treated by CXL only remained stable.

**Conclusion:** PRK after CXL might be a treatment option in particular cases, however, with the risk of re-progression. More information is needed about indications and contraindications of this approach.



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5 **Keratoconus exacerbation after cross-linking and surface ablation –**  
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7 **a case report**  
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56 Commercial interests: None  
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3 Abstract  
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5 **Purpose:** Topography-guided photorefractive keratectomy (PRK) in cases of forme fruste  
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7 keratoconus is considered a treatment option for optical rehabilitation. Recently this approach  
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9 was proposed for keratoconus corneas after corneal cross-linking (CXL). We report a case where  
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11 the photoablation reinitiated progression of keratoconus.  
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14 **Patient and methods:** A patient with bilateral keratoconus underwent bilateral CXL with a  
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16 stabilization of corneal topography after treatment. Customized PRK (topography-guided) was  
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18 performed in the left eye at 2 years after CXL.  
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21 **Results:** Immediately after PRK the eye showed progression of the keratoconus, whereas the  
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23 right eye treated by CXL only remained stable.  
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26 **Conclusion:** PRK after CXL might be a treatment option in particular cases, however, with the  
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28 risk of re-progression. More information is needed about indications and contraindications of this  
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30 approach.  
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4 Biomechanical [1] and biochemical [2] properties of the cornea can be modified by means of  
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6 cross-linking using ultraviolet (UV) light in combination with riboflavin (CXL). This treatment  
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8 stiffens the cornea and as a consequence may inhibit progression of keratoconus [3] or iatrogenic  
9  
10 keratectasia [4]. Other promising applications of corneal cross-linking (CXL) are currently under  
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12 investigation such as arrest of corneal melting [5], reduction of corneal stroma edema in Fuchs  
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14 dystrophy [6], and CXL in combination with intrastromal rings [7].  
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21 Once the progression of keratoconus is stopped after CXL there is still the question of optical  
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23 rehabilitation. Although most of the patients can go back to contact lenses in some cases of  
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25 contact lens-intolerance alternatives of optical rehabilitation are necessary such as intrastromal  
26  
27 rings and shallow surface ablation. Kanellopoulos [8] recently reported a case of successful PRK  
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29 treatment in a keratoconus eye that had previously been cross-linked.  
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35 In this case report, we present a keratoconus patient with successful stabilization of the cornea  
36  
37 after CXL for more than two years and with immediate re-progression of keratoconus after a  
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39 subsequent PRK.  
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3 Patient and Methods  
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7 A 21 year old male patient suffering from keratoconus underwent CXL in both eyes in 2004 at  
8 the University Eye Clinic, Dresden, Germany. Keratoconus progression was documented in the  
9 years before CXL by Scheimpflug topography (Pentacam, Oculus, Wetzlar, Germany).  
10  
11

12 Postoperative topography documented a halt in progression of keratoconus during 2 years after  
13 CXL. Uncorrected visual acuity (UCVA) was 20/100 in the right eye and 20/200 in the left eye  
14 and best spectacle-corrected visual acuity (BSCVA) was 20/40 OD (manifest refraction -1.75 cyl  
15 -1.0 X 20) and 20/40 OS (manifest refraction -0.5 cyl -3.0 X 180). By means of a pin hole,  
16 BSCVA was 20/30 in both eyes. Slit lamp examination revealed discrete anterior stromal scarring  
17 in both eyes and Vogt -striae in the left eye, but no demarcation line. Corneal ultrasound  
18 pachymetry (SP-2000, Tomey, Nagoya, Japan) yielded a central thickness of 460µm in the right  
19 and 405µm in left eye with a thinnest reading of 385µm at the cone peak. Corneal topography  
20 (Pentacam, true net power, Fig. 1a) demonstrated a typical keratoconus with steepest K-readings  
21 of approximately 56 D in both eyes. The patient could neither tolerate rigid nor soft contact  
22 lenses and was not satisfied with the visual acuity obtained with glasses. Treatment alternatives  
23 such as intrastromal rings and deep lamellar keratoplasty were discussed but the patient preferred  
24 a shallow surface ablation for his non-dominant left eye with the perspective that a deep lamellar  
25 keratoplasty was still an option even if keratoconus progression would be reinitiated by the  
26 ablation.  
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3 CXL  
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5 CXL was performed at the Department of Ophthalmology of the University Hospital Dresden,  
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7 Dresden, Germany using an early version of the treatment parameters [3] differing from the  
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9 currently used technique in a shorter application of riboflavin of only 10 minutes. All other  
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11 parameters such as irradiation time, UV fluence, wavelength, riboflavin concentration and  
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13 medical postoperative management were similar to the current standard procedure [9].  
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19 PRK  
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21 After a manual abrasion of the epithelium ultrasound pachymetry yielded a stromal thickness of  
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23 355 microns at the thinnest point. A customized surface ablation (T-CAT, WaveLight, Erlangen,  
24  
25 Germany) based on Scheimpflug imaging was performed with an optical zone of 5.0 mm in  
26  
27 diameter and an attempted hyperopic correction of +5.0 cyl -3.0 X 179 aiming on a target  
28  
29 refraction of approximately -4.0D. The strong hyperopic treatment was used to save tissue in the  
30  
31 central cornea and at the cone peak [10]. The photoablation was achieved with the Concerto  
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33 excimer laser (WaveLight, Erlangen, Germany) working at a repetition rate of 500 Hz. At the end  
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35 of the treatment, mitomycin 0.02% was applied for 30 seconds followed by irrigation with chilled  
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37 balanced salt solution. After the treatment, a bandage lens soaked with 0.3 % preservative-free  
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39 ofloxacin (Floxal UD, Chauvin Novopharma AG, Steinhausen, Switzerland) was applied and  
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41 Floxal drops were applied until the epithelium was healed.  
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3 Results  
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5 The right eye with CXL only continued to demonstrate stable corneal topographies.  
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7 Prior to the photoablation performed at 2.5 years after CXL, the left eye showed similar findings.  
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10 Already 3 days after PRK at the slit lamp a protrusion of the central cornea was visible and at one  
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12 month post PRL keratoconus had clearly progressed (Fig. 2b) with a BSCVA of 20/200 (manifest  
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14 refraction -4.0 cyl -5.0 X 170). This progression continued until 6 months after PRK as  
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16 documented by corneal topography (Fig. 2c) and refraction (BSCVA of 20/200 with a manifest  
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18 refraction of -12.0 cyl -6.0 X 05). At this point we proposed a deep lamellar keratoplasty.  
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3 Discussion

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5 Cases of forme fruste keratoconus (achieved naturally or by means of CXL) and contact lens  
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7 intolerance have not many options to achieve a sufficient visual acuity. Spherocylindrical  
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9 spectacle correction cannot compensate for the irregular component of the astigmatism and  
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11 keratoplasty is not yet appropriate regarding the relatively good BSCVA of 20/40 [10]. The  
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13 remaining alternatives include intrastromal rings and surface ablation.  
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19 The main problem of surface ablation after CXL is an unknown requirement regarding the  
20  
21 residual thickness of the stromal bed to prevent progression of the keratoconus cornea. Only few  
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23 cases are reported with surface ablation in formes frustes of keratoconus [11] and only one case  
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25 was so far presented with customized PRK after CXL[8]. Corneal cross-linking is a treatment  
26  
27 option for progressive keratectasia with small complication and failure rates [12] because  
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29 stiffening of the extracellular matrix a biomechanical stabilization of the cornea is obtained. In  
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31 other words, the progressive form of a keratoconus is turned into its abortive form, the forme  
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33 fruste. The cross-linking effect is limited to the anterior corneal stroma up to a depth of 270 to  
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35 330  $\mu\text{m}$  [13]. Since also in the normal human cornea, the anterior stroma has a higher  
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37 biomechanical strength compared to the posterior part [14] CXL reestablishes the natural  
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39 stiffness-gradient across the keratoconus cornea. Experimental data demonstrated that the  
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41 biomechanics of the keratoconus cornea is probably a factor of 2 weaker compared to the normal  
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43 cornea [15]. On the other hand, corneal rigidity is increased after CXL by a factor 4 [14].  
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50 Therefore, CXL may compensate for the biomechanical weakness of the keratoconic cornea.  
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3 In regular corneas gross estimations led to a minimal residual stromal thickness after LASIK of  
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5 250 $\mu\text{m}$  [16]. Later on, cases of iatrogenic keratectasia in corneas thicker than 250  $\mu\text{m}$  were  
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7 reported [17] and today we recommend a residual stromal thickness of 300 microns.  
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10 In analogy, in keratoconic eyes after CXL a minimal residual stromal thickness of at least 300  
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12  $\mu\text{m}$  could be assumed to maintain corneal stability and to prevent keratoconus progression.  
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15 In the case presented the corneal thickness at the thinnest point was 355  $\mu\text{m}$  after epithelium  
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17 removal. Fig. 2a demonstrates the ablation pattern for the target emmetropia with an ablation  
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19 depth of approximately 48 $\mu\text{m}$  at the point of thinnest stroma. Adding some hyperopia correction  
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21 aiming on a target myopia of -4.0D the ablation depth at the thinnest point is only 16 $\mu\text{m}$  (Fig 2b).  
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24 The residual stromal thickness in this case is still 340 $\mu\text{m}$  and, therefore, we speculated the  
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26 thickness to be sufficient even after PRK treatment to maintain corneal stability. However, the re-  
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28 progression of keratoconus suggest an insufficient residual stromal thickness or an inadequate  
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30 biomechanical strength of the cornea although CXL was performed.  
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36 Forme fruste keratoconus (FFKC) may serve as a model for the keratoconus cornea post CXL. In  
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38 FFKC the cornea has regained its biomechanical stability without surgical intervention most  
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40 probably due to an age-related increase in collagen cross-links [19]. In such cases, surface  
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42 ablation can help to improve the optical homogeneity of the corneal surface [11, 19, 20].  
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46 However, strict inclusion criteria were accepted in the small pilot series of patients presented:  
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48 among others residual central corneal thickness (ultrasound) was higher than 450 microns and the  
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50 ablation depth was less than 50 microns [11]. Comparing these inclusion criteria of our study on  
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52 surface ablation in FFKC with the case presented here, we fell short regarding age (21 years  
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54 instead of >25years), corneal thickness (385 $\mu\text{m}$  instead of >500 $\mu\text{m}$ ), residual stromal thickness  
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56 (325 $\mu\text{m}$  instead of >450  $\mu\text{m}$ ) and K-readings (56D instead of <49D). The outcome of this case  
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3 indicates that the lower limit of 450  $\mu\text{m}$  for residual corneal thickness applied in FFCK-cases  
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5 (450 $\mu\text{m}$ ) should also be maintained after CXL rather than that of normal corneas (300 $\mu\text{m}$ ).  
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10 Another reason for the failure in this patient may be insufficient corneal stiffening due to the  
11  
12 inappropriate CXL technique. The current protocol of riboflavin/UVA cross-linking includes  
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14 riboflavin application for 30 minutes prior to UV-irradiation [9]. An application time of only 10  
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16 minutes (as performed in this case) significantly reduces the intrastromal riboflavin concentration  
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18 and, therefore, radical formation rate and number of cross-links [9].  
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24 In summary, we present a case of successful CXL in a cornea with progressive keratoconus. After  
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26 surface ablation with only minimal ablation depth over the thinnest area of the cornea the  
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28 keratoconus decompensated and significant progression occurred. Before using surface ablation  
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30 as a standard option after CXL, better recommendations for inclusion criteria especially the  
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32 residual stromal thickness have to be established.  
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3 Legends

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5 Fig. 1

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7 (1a) Corneal topography at 2 ½ years after CXL (arrow indicates thinnest point of the cornea)  
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9 prior to PRK. (1b) Corneal topography of the same eye at 1 month and (1.c) at 6 months after  
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11 PRK .  
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17 Fig. 2

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19 Topography-guided ablation pattern with target refraction emmetropia (2a) and myopia of -4.0 D  
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21 (2b). The ablation depths shown in the lower right corner (act) indicate the ablation at the thinnest  
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23 point.  
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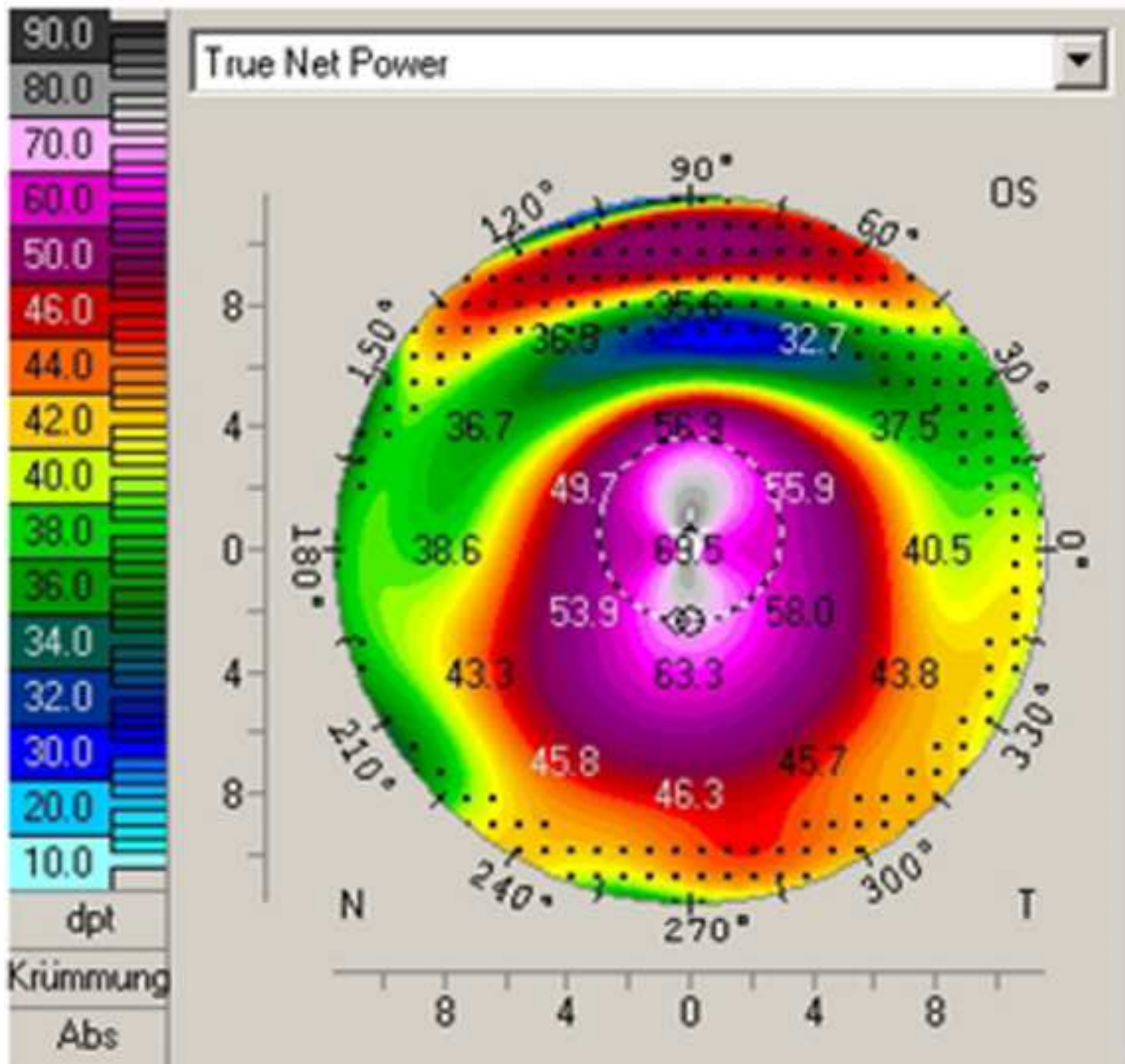


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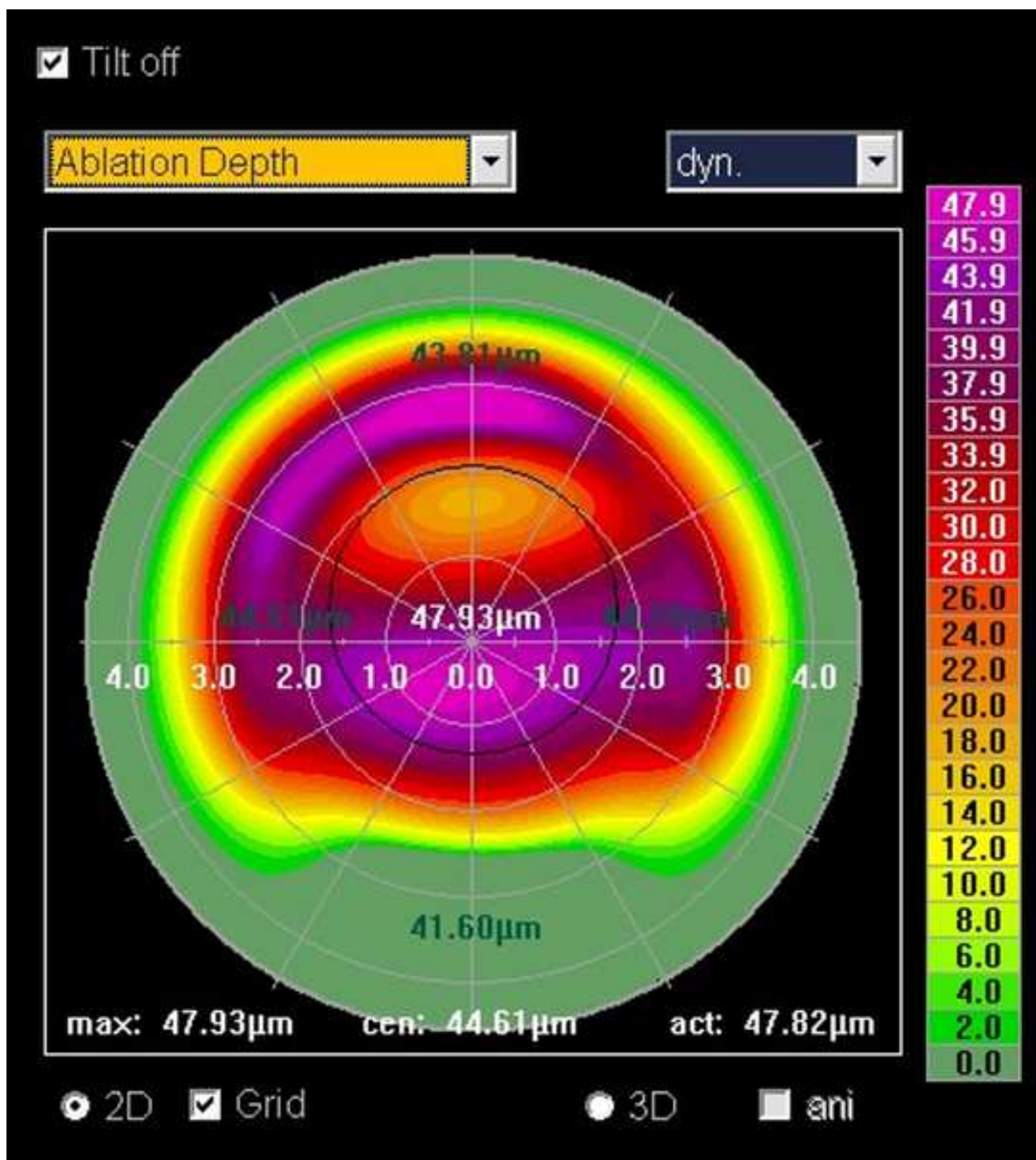


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