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# **Effect of Nd:YAG capsulotomy on the morphology of surviving Elschnig pearls**

Nino Hirschall, MD <sup>1, 2</sup>

Thomas Neumayer, MD <sup>2</sup>

Michael Georgopoulos, MD, MBA <sup>2</sup>

Oliver Findl, MD, MBA <sup>1, 2</sup>

<sup>1</sup> Moorfields Eye Hospital, London, United Kingdom

<sup>2</sup> Dept. of Ophthalmology, Medical University of Vienna, Vienna, Austria

Corresponding author and reprint requests:

Oliver Findl, MD, MBA

Moorfields Eye Hospital NHS Foundation Trust

City Road

London EC1V 2PD

United Kingdom

oliver@findl.at

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Competing Interest: None declared.

## Abstract

**Purpose:** To observe the short-term changes in morphology of Elschnig-pearls induced by Nd:YAG-capsulotomy.

**Setting:** Department of Ophthalmology, Medical University of Vienna, Austria

**Method:** Twenty eyes of 19 pseudophakic patients with regenerative posterior capsule opacification (PCO) that were scheduled for YAG-capsulotomy were included in this prospective study. High resolution digital retroillumination images were taken 2 weeks, 1 week and shortly before and immediately, 1 week and 2 weeks after Nd:YAG-capsulotomy. The series of images were analysed using a dedicated image analysing software (PearlTracer).

**Results:** In total 2431 Elschnig-pearls were observed over the time-course of 4 weeks in this study. Of these 535 pearls (30.6%) disappeared and 503 pearls (27.6%) survived on the remaining capsule peripheral to the capsulotomy-opening. The surviving pearls showed a significant decrease in size (20%) from immediately before to 10 minutes after capsulotomy.

Within the first weeks after capsulotomy there was a high number of newly appearing pearls, with 26% of all pearls being new between 1 and 2 weeks indicating high pearl turn over.

**Conclusion:** Capsulotomy had immediate impact on the morphology of PCO outside the capsulotomy opening, probably due to the direct mechanical impact of the laser shockwave.

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Improvements in intraocular lens (IOL) –design<sup>1,2,3</sup> and surgical technique diminished PCO (Posterior capsule opacification, secondary cataract, after-cataract) rates, but PCO is still the most frequent long-term side effect and the main reason for a decrease in visual acuity and loss of contrast sensitivity after cataract surgery<sup>4</sup>.

In recent studies highly dynamic morphological changes of Elschnig pearls were observed over short periods of time<sup>5,6</sup>. Georgopoulos and co-authors<sup>2</sup> observed a spontaneous regression of Elschnig pearls after YAG-capsulotomy with disappearing of pearls on the remaining capsule in 45% of the cases in a long-term follow-up study. However, it remains unclear when and why the pearls outside the capsulotomy opening undergo these changes. Capsulotomy could be used as a model of mechanical destruction by the shockwave on surrounding, “by-standing” pearls.

Aim of this study was to assess the morphological changes of Elschnig pearls immediately after capsulotomy. This knowledge may lead to a better understanding of the pathogenesis of PCO and so may help to develop new strategies of controlling PCO. This is of special interest since PCO remains the main problem of lens refilling (Phakoersatz) for restoration of accommodation.<sup>7</sup>

## **Material and methods**

### *Study design:*

The patients were included in a continuous cohort as they appeared in the outpatient clinic at the Department of Ophthalmology (Medical University of Vienna, Vienna, Austria). Inclusion criterion was the necessity of Nd:YAG-laser capsulotomy because of regenerative PCO (pearl-type) in one or both eyes. Exclusion criteria were tear film problems, corneal pathology as well as dense vitreous opacities to

avoid artifacts in the retroillumination images. Furthermore patients with fibrotic PCO or mixed PCO were excluded from this study.

Posterior capsulotomy was performed with a Nd:YAG-laser (Visulas YAG II, Zeiss, Jena, Germany). After dilating the pupil, the capsule was opened downwards along the vertical meridian and then along the horizontal meridian. After the YAG-capsulotomy the patients received ketorolac 0.5% (Acular, Allergan, Irvine, CA) eye drops 3 times daily for 4 weeks.

All the research and measurements followed the tenets of Helsinki. Informed consent was obtained from all patients prior to the procedure.

#### *Image acquisition and analysis*

To document even minor changes in morphology of Elschnig-pearls we used a high-resolution digital retroillumination system<sup>8</sup> which was specifically used for PCO assessment at our institution (Digital Coaxial Retroillumination Photography, DCRP). The optical system consists of a 30 SL-M slit-lamp and a retrolux illumination module with illumination provided by a flash pack through a fiberoptic cable (all Carl Zeiss Meditec GmbH, Jena, Germany). This system allows coaxial illumination imaging. A digital color camera (Kodak NC2000, Rochester, NY) was connected to the system. The images were directly transferred to a personal computer and imported into the program Photoshop 7.0 (Adobe, San Jose, USA).

Our image acquisition system produced high-quality digital images of the posterior capsule and was shown to have a high reproducibility.<sup>8</sup>

Six digital retroillumination images were taken 2 weeks, 1 week and 10 minutes before YAG-capsulotomy, and 10 minutes, 1 week and 2 weeks after YAG-capsulotomy in a standardized fashion by two experienced examiners. The patient

was asked to look straight into the collimated light. Several images of the posterior capsule were taken (magnification: 12 x) and images of best quality (focus, exposure, position of reflexes) were stored on hard-disc and imported into MATLAB 7.0.4. (The Mathworks Inc., Natick, United States). With the MATLAB software and a dedicated plug-in (PearlTracer 1.0 developed by the Technical University of Graz), the series, of all 6 images of each eye was created. Within these series, single Elschnig pearls were traced from image to image. To mark the outlines of a pearl the observer could choose between 3 features: 1. Snake selection: where the observer marked a few points on the outlines of the pearl and the program detect the pearl border automatically. 2. Diameter circle selection: where the observer chose a circle function and adapted it in size most appropriate, when the pearl was circular. 3. Polygon selection: where the observer marked several points on the outline of the pearl and these points were then connected by straight lines.

Each pearl, the YAG-opening and the pupil were marked and identified by a number (Figure 1). The analysis was always started from the first image to the last image of the series. Then the non-marked pearls in the last image were traced backwards towards the earlier images. Finally the middle images were checked for non-marked pearls, which would have been newly appearing and disappearing pearls within the 4 weeks of observation. Pearls which were not visible in one or more images because of Purkinje reflexes from the co-axial illumination were excluded from the analysis in all images. After the marking of the entire series was completed the program generated an Excel file. The file contained the consecutive identification numbers of the marked pearls and their sizes in pixels on each follow-up image. For statistical evaluation the data was imported into SPSS<sup>®</sup> for Windows 14.0 (SPSS Inc., Chicago, Illinois, United States).

To convert the values from pixels into  $\mu\text{m}^2$ , we measured the known diameter of an IOL (6mm) and calculated the conversion factor to compensate for the magnification factor of our photographic system.  $1 \text{ Pixel} = 6.325\mu\text{m} \times 6.325\mu\text{m} = 40\mu\text{m}^2$

To assure that the remaining contact gel from the YAG-capsulotomy on the corneal surface had no optical influence on the analysed pearls we measured the constant length (distance between the haptics) before and after YAG-capsulotomy. No difference was found for magnification between the preYAG image without contact gel and the postYAG image with contact gel, by measuring IOL diameter to the nearest 50 micrometers using image analysis software in these serial photographs. By evenly distributing the pearls from all pre-capsulotomy images into 3 groups, we defined the following size categories:

- small pearls:  $50\mu\text{m}^2$  -  $2800\mu\text{m}^2$
- medium pearls:  $2801\mu\text{m}^2$  -  $7250\mu\text{m}^2$
- large pearls:  $7251\mu\text{m}^2$ , or larger

Note that the smallest detectable pearl using our setup was in the order of  $50\mu\text{m}^2$ .

To classify pearls, the size and position of the YAG-opening in the image taken 10 minutes after YAG-capsulotomy was inserted into the image taken just before capsulotomy in every series. Accordingly, the pearls were classified as “disappearing pearls inside the YAG-opening”, “disappearing pearls on the remaining (peripheral) capsule”, and “surviving pearls”, shown in figure 2. Morphological changes, such as appearing, disappearing, increasing and decreasing in size as well as fusing and separating of pearls were observed.

### *Evaluation of Elschmig pearl density*

The smallest pupil size was used to define the area of analysis in the other images of every series. In all images the area of the YAG-opening was subtracted from the area of the smallest pupil to analyse same sized areas.

The pearl density in ‰ was calculated as followed: the total area of all marked pearls in the processed image divided by the area of the smallest pupil x 1000.

### *Evaluation of YAG-energy*

To calculate the Energy, we multiplied the number of shots with the energy used in mJoule.

### *Reproducibility*

Neumayer et al.<sup>9</sup> already analysed the intra-observer reproducibility of the semi-objective image analysing software. To assess the inter-observer reproducibility, a 10-image-serie was marked by two observers. From the first observer, 125 numbered pearls (out of 4 images of 4 different patients) were randomly selected and identified in the images of the second observer. The differences in pearl size between the two observers were analyzed.

## **Results**

Twenty eyes of 19 patients were included in a continuous cohort during 4 months. All patients underwent cataract surgery 2 to 4 years before attending our clinic. The mean age was: 71.0 years (range: 44 – 86). A total of 2431 pearls were analysed during the entire observation time, of which 1768 pearls were present immediately before the YAG-capsulotomy. None of the patients in this study was lost to follow-up.

Concerning numbers of pearls, all 730 pearls disappeared from inside the capsulotomy opening, as expected. This number constitutes 42% of all pearls of all eyes within the mean capsulotomy area of  $7.9\text{mm}^2$  (SD:  $0.3\text{mm}^2$ , range:  $4.09\text{mm}^2$  to  $15.2\text{mm}^2$ ).

On the remaining capsule outside of the capsulotomy opening, 535 pearls (30.2% of all pearls, range: 12% to 58.3%) disappeared. The surviving pearls (503 pearls) were distributed evenly among the categories of pearl size with nearly equal numbers of small, medium and large pearls (33% each), shown in figure 3.

Of all pearls, 22 pearls (0.9%) appeared to show fusion and 14 pearls (0.6%) appeared to separate during the observation time of 4 weeks.

Concerning morphological changes outside the capsulotomy opening the mean pearl size changes are shown in table 1.

The only significant change in pearl size was found immediately after capsulotomy from  $8550\mu\text{m}^2$  to  $6850\mu\text{m}^2$  a 20% decrease (range:  $40\mu\text{m}^2$  to  $18640\mu\text{m}^2$ ,  $p < 0.05$ , ANOVA).

		Pearl size: Mean in $\mu\text{m}^2$ (SD) <sup>1</sup>				Density <sup>2</sup>
		All sizes	Small	Medium	Large	In ‰ (SD)
Before capsulotomy	2 weeks	8850 (14170)	2910 (4260)	5240 (4080)	16970 (19290)	22.5 (12.7)
	1 week	8310 (13290)	2450 (2260)	4950 (3570)	17600 (20040)	22.14 (15.1)
	preYAG	8550 (13810)	1670 (640)	4570 (1290)	19980 (19740)	29.3 (20.1)
After capsulotomy	postYAG	6850 (15040)	2070 (2650)	3620 (3660)	15060 (24460)	10.8 (10.1)
	1 week	8590 (14360)	3250 (3310)	5920 (7750)	17590 (25290)	14.9 (13.0)
	2 weeks	8990 (13310)	5430 (10910)	6520 (7600)	14840 (20390)	14.1 (14.0)

**table 1**

Pearl size and area of surviving pearls in the region outside of capsulotomy opening before and after capsulotomy

<sup>1</sup> Pearl size at pre-capsulotomy image was used to allocate into size category

<sup>2</sup> Percentage of pearl area as part of entire analysed area in ‰

The percentage change in size was more pronounced for small pearls (43%) as compared to medium and large pearls (20%, Cohen's  $d=0.29$ ).

Concerning the pearls that disappeared outside the capsulotomy opening, they appeared to have been the more stable pearls concerning change in size in the 2 weeks prior to capsulotomy. The change in pearl size for these disappearing pearls was 5.5% compared to the surviving pearls 3.3% (Cohen's  $d=0.24$ ).

All eyes with more than 20‰ pearl density before the YAG-capsulotomy showed a decrease in pearl density 10 minutes after YAG- capsulotomy, which was significant (more than 50% of cases,  $p<0.05$ , paired T-Test)".

Concerning the effect of the Nd:YAG-laser energy on pearl changes, no correlation was found between the laser energy and the amount of disappearing pearls ( $r^2=0.29$ ,  $p=0.24$ , Pearson). A mean energy level of 1.5mJ was used for the YAG-capsulotomy (range: 1.1mJ to 2.4mJ).

There was a high inter-observer reproducibility with a correlation of  $r^2= 0.969$ , ( $p< 0.05$ , T-test for paired samples) for pearls marked by two different observers (Figure 4). Inter-observer and intra-observer reproducibility were within the limits of agreement.

Neither age, nor gender had significant influence on the morphological changes of Elschnig pearls after YAG-capsulotomy.

## Discussion

Aim of this study was to observe the morphological changes of Elschnig pearls before and after YAG-capsulotomy. A data set of 120 retroillumination images of 20 eyes with regenerative PCO before and after YAG-capsulotomy was created. A sophisticated optical setup allowed us to examine the morphology of PCO structures in fine detail. The high quality of the images was essential for this study.<sup>10</sup>

We observed that a similar percentage of pearls outside the capsulotomy opening that disappeared and survived the capsulotomy. The number of disappeared pearls on the remaining capsule was several orders of magnitude higher than the normal turn-over of pearls, especially taking into account that this change was observed in a short time span of only 20 minutes.

Georgopoulos and co-authors<sup>2</sup> mentioned a spontaneous regression of Elschnig pearls after YAG-capsulotomy with a loss of pearls on the remaining capsule in 45% of the cases. Reduced contact between the posterior capsule and the IOL surface might facilitate posterior migration of the cells towards the margin of the posterior capsulotomy opening and, in consequence, the pearls may fall into the vitreous cavity. Another possible explanation could be the direct mechanical detonation of the laser shockwave. A higher number of disappearing pearls around the YAG-opening would be expected compared to pearls more peripheral in location. However, although pearls that were adjacent to the rhexis showed a slightly higher stability, no significant differences were found concerning the distance to the YAG-opening and number of disappearing pearls. We found no correlation between YAG-laser energy

used and the size changes. However, the range of energy used did not vary significantly between most eyes. Alternatively, apoptosis of the cells might be induced by cytokines of the aqueous humor, which has gained access to the LECs through the opened posterior capsule, although this would be expected to take longer than just minutes. Also phagocytosis of pearls by macrophages, probably having immigrated from the vitreous, could cause these changes.<sup>13</sup> Alternatively, osmotic processes could lead to bursting of cells when aqueous from Berger's space rushes into the subcapsular room once the capsule is opened.

Many new pearls appeared within the first week after YAG-capsulotomy. Probably the increase in space between the posterior capsule and the IOL due to the released tension in the posterior capsule after capsulotomy lead to the higher number of newly formed pearls. Another possible reason for this increase in the number of Elschnig pearls could be an inflammatory process following the capsulotomy. Probably these newly formed pearls migrate towards the capsulotomy margin in the weeks and months after capsulotomy to form an accumulation of pearls at the capsulotomy margin, called pearl strings. However, the observation period of this study was too short to observe the creation of pearl strings. Kurosaka et al.<sup>14</sup> and Kato et al.<sup>15</sup> observed an appearance of pearl strings in 70% of all eyes one to two years after Nd:YAG-capsulotomy, analysing 201 eyes and 418 eyes.

The remaining pearls showed a sudden decrease in size and displayed a significantly increased turnover during the weeks following capsulotomy. This decrease could be due to the fact that the pearls were flattened between the posterior capsule and the surface of the IOL. After YAG-capsulotomy the space between the posterior capsule and the IOL-surface is larger and the pearls change

from a flattened into a more spherical shape. Even though the volume of the pearls may stay constant the pearls appear smaller on the 2D-image. Back calculating from a spherical pearl after capsulotomy to an anterior-posterior compression of about 10% of pearl thickness caused by the taut posterior capsule would be necessary. To prove this, a 3-dimensional scanning of the pearls would be necessary. Alternatively, as mentioned above, osmotic changes due to an altered milieu in the sub-capsular region around the pearls as a result of aqueous inflow from Berger's space could cause a rapid change in pearl size. This change in milieu would need to be hyperosmolar compared to the usual capsular bag milieu.

Neumayer<sup>9</sup> and co-authors already analysed the intra-observer reproducibility of the semi-objective image analysing software and found a high intra-observer reproducibility: a total of 100 pearls of 5 different patients were selected and marked again by the same observer 3 months after the original evaluation had been performed. Intra- and inter-observer reproducibility of the evaluation method used was high.

The clinical importance of these findings may be to attempt to find new strategies of laser 'polishing' PCO without opening the posterior capsule. This would allow non-invasive removal of PCO and its symptoms, but leave the posterior capsule intact which acts as a border between anterior and posterior segment. This may lead to a reduction of the complications described for YAG-capsulotomy such as increases in intraocular pressure, cystoid macular edema and retinal detachment. Additionally, leaving the capsule intact would be helpful in cases of vitreoretinal surgery with silicone oil, or in cases where an IOL exchange may be necessary at a later date. Such a scenario of deciding on IOL exchange or PCO treatment is becoming more

common with the increased use of multifocal IOLs. Some patients report poor visual function which may be the result of the inherent problems of multifocal technology, such as increased glare and decreased contrast sensitivity, but may also be the result of slight PCO which enhances these optical shortcomings. The surgeon needs to decide whether the IOL needs to be exchanged for a monofocal IOL, or a capsulotomy may reduce the symptoms for the patient. However, once the posterior capsule is open, a vitrectomy would be necessary if an IOL exchange does need to be performed thereafter, putting the patient at an increased risk of postoperative complications such as retinal detachment and cystoid macular edema.

On the basis of our high quality images of the posterior capsule of pseudophakic eyes we were able to analyze the change in morphology of PCO before and immediately after capsulotomy in fine detail with high resolution and precision. To our knowledge, this is the first study with a systematic analysis of the immediate effect of the Nd:YAG laser on the morphology of pearls. For a more complete understanding of the morphological changes of Elschnig pearls, 3-dimensional imaging, such as high resolution optical coherence tomography, may be helpful in the future. The findings of this study about collateral damage of Elschnig pearls from Nd:YAG laser capsulotomy may be of relevance for designing new laser treatment strategies for PCO in the future that preserve the posterior capsule.

## Legends

### figure 1

Screenshot of PearlTracer software to analyse image series. Pearls traced and identified by number.

### figure 2

Retroillumination images were taken 10 minutes before (upper image) and 10 minutes after (lower image) capsulotomy. On the remaining posterior capsule outside the opening (arrows) pearls disappeared (inside the circle), or survived (inside the rectangle).

### figure 3

Change of appearing (black bars) and disappearing (grey bars) pearls on the remaining capsule area outside capsulotomy opening of all 20 eyes at each follow-up (2431 pearls analysed)

### table 1

Pearl size and area of surviving pearls in the region outside of capsulotomy opening before and after capsulotomy

### figure 4

Pearl sizes analysed by two different observers at different times to prove the inter-observer reproducibility

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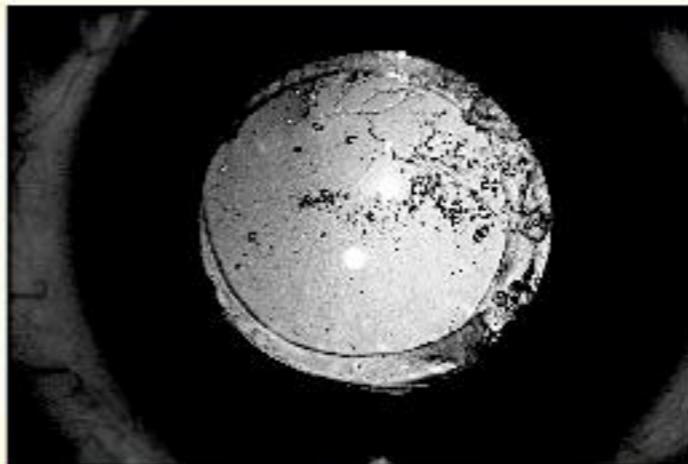
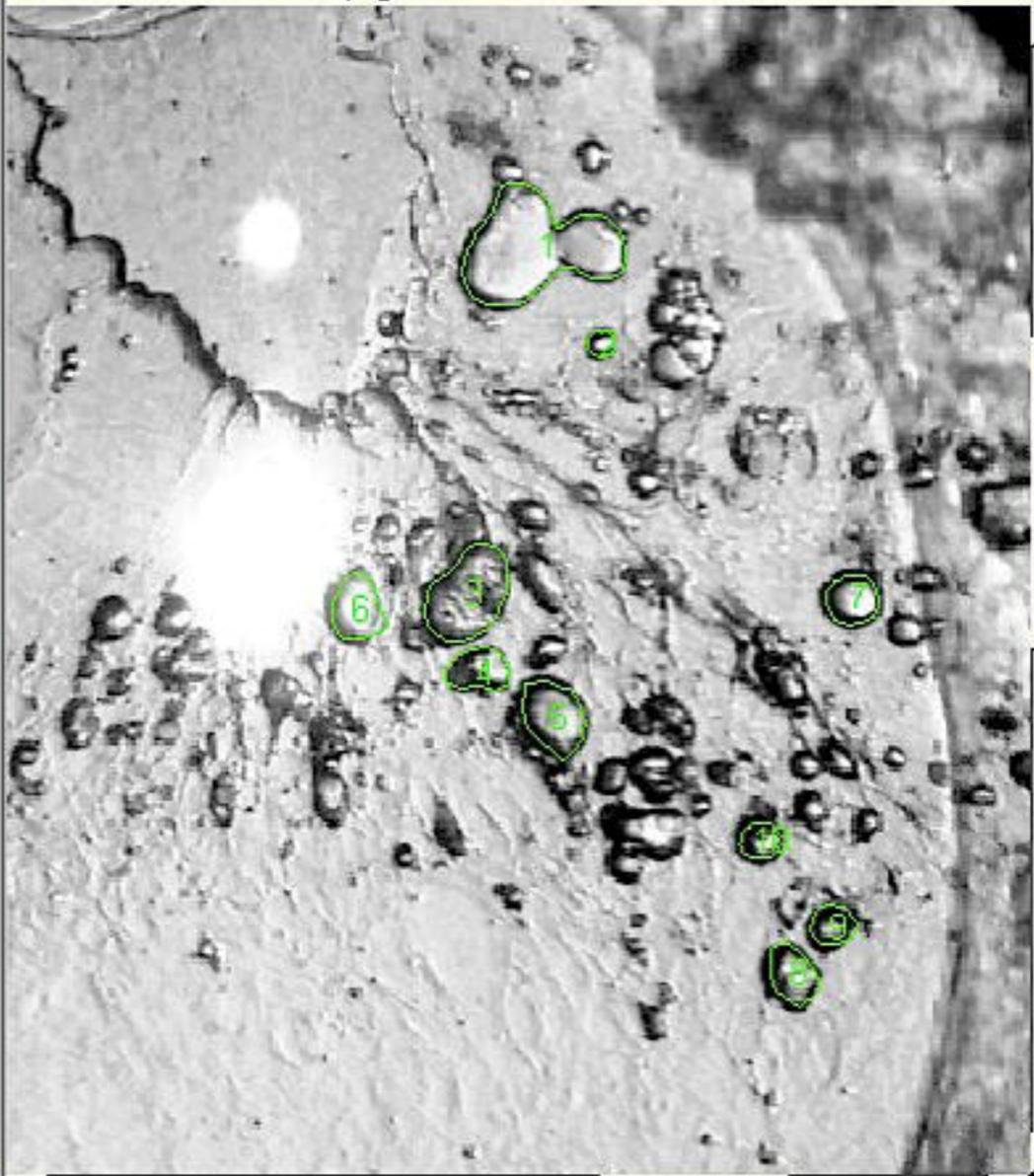
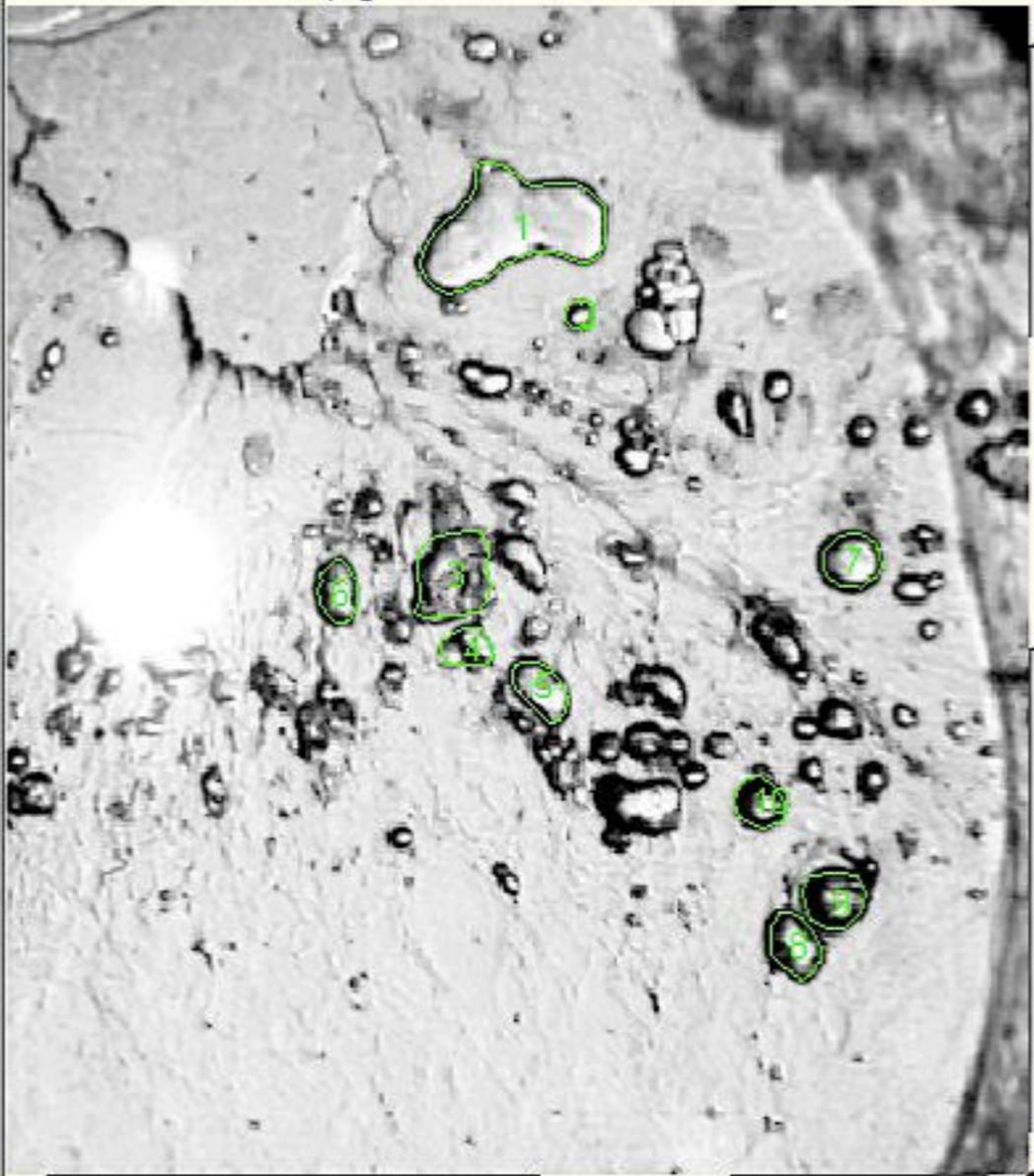
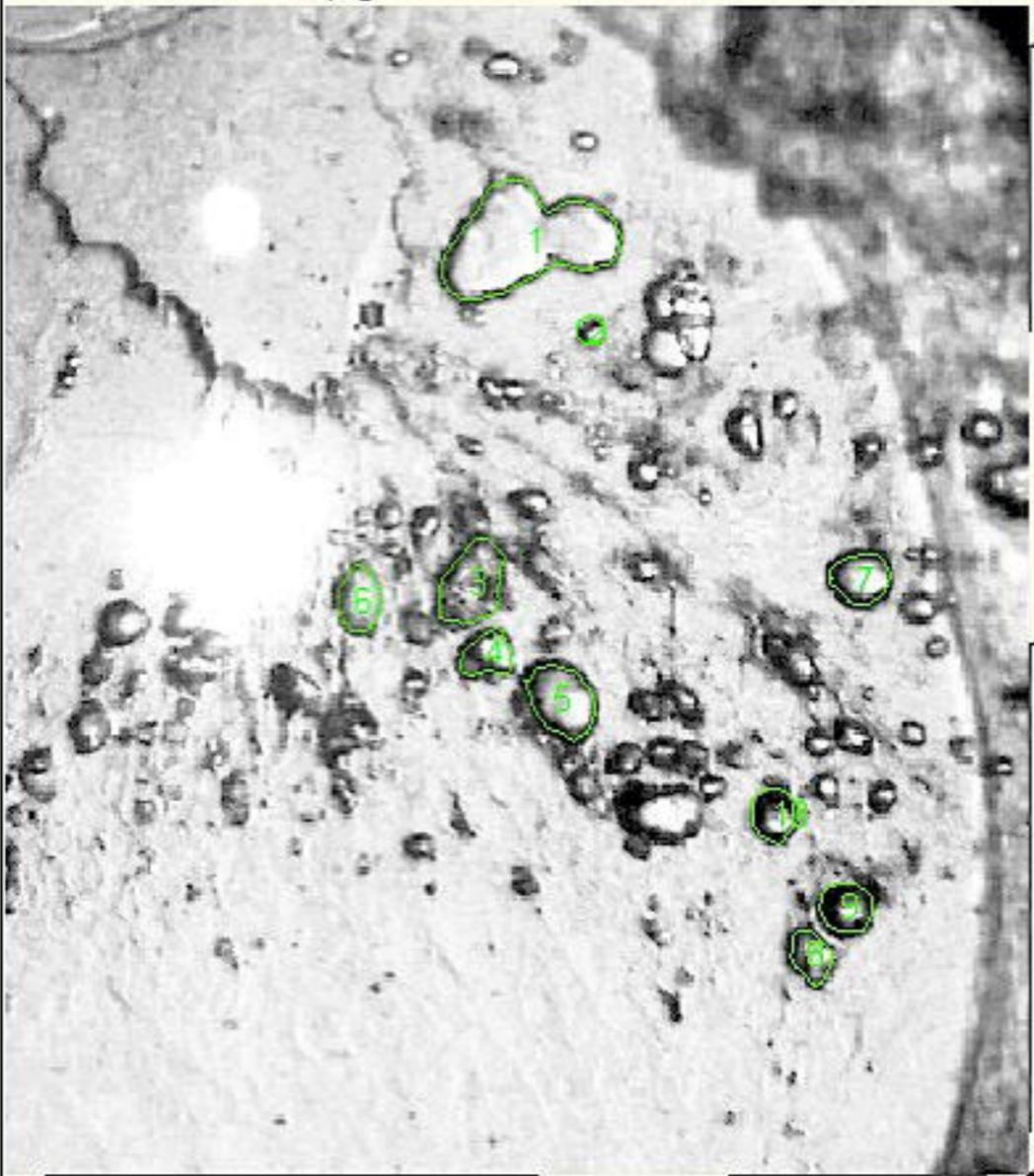
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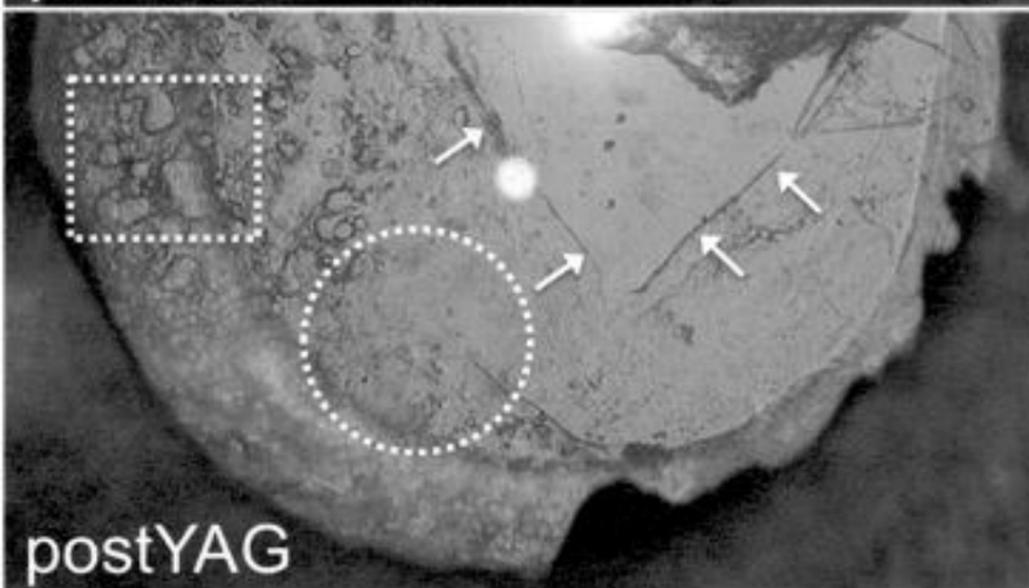
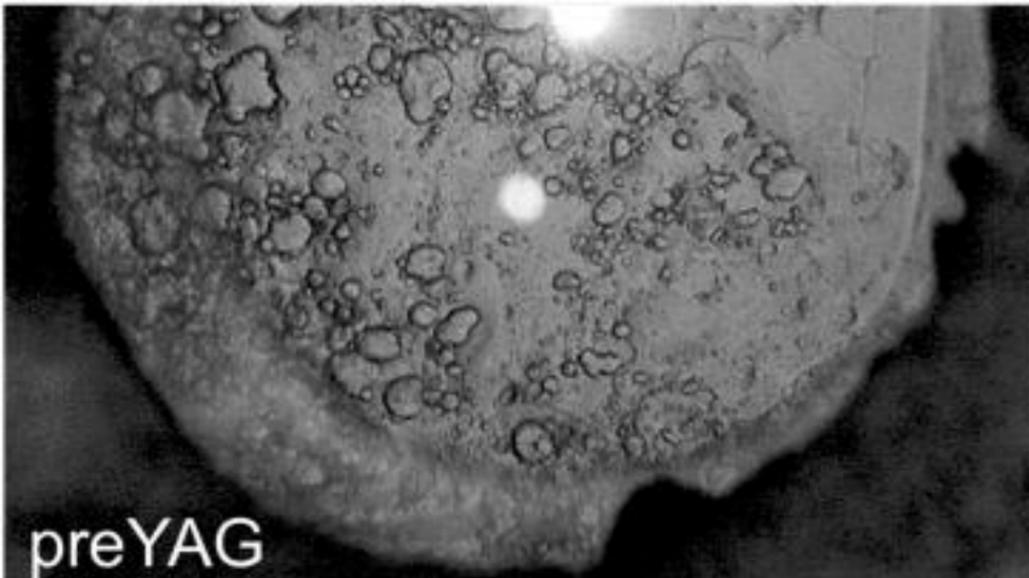
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### Number of pearls between the follow ups of disappearing and appearing pearls

