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Adhesion and mechanical properties of nanocrystalline hydroxyapatite coating obtained by conversion of atomic layer deposited calcium carbonate on titanium substrate

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ABSTRACT

The purpose of this study was to evaluate the mechanical properties of nanocrystalline hydroxyapatite coating by tensile adhesion testing and scratch testing. The coating was manufactured on titanium substrate by converting atomic layer deposited (ALD) calcium carbonate thin film in dilute phosphate solution. The tensile adhesion testing was performed with hydraulic testing device in accordance with ISO 4624 and ISO 16276-1. Scratch testing was done according to SFS-EN 13523-12 with spherical ø10 µm scratching tip. Characterization of the samples was done with light and electron microscopy after which they were stained with alizarin red and the failure modes and loadings were analyzed.

The highest obtained tensile adhesion value was 6.71 MPa produced with 4000 ALD cycles, converted to hydroxyapatite in alkaline solution and annealed for 30 min in 700°C. The annealing improved the adhesion values by approximately 0.8 MPa, but examining the samples with electron microscopy showed intact coating in both annealed and non-annealed samples. Samples produced with 4000 cycles performed better in testing than 2000 cycle samples, and better adhesion was also achieved with alkaline conversion solution compared to neutral solution.

Keywords: hydroxyapatite, calcium carbonate, adhesion, atomic layer deposition, titanium

1. INTRODUCTION

The number of joint replacement surgeries has increased over the last few decades along with aging population and prolonged life expectancy. This has created a need for developing current implant technologies to improve osseointegration and implant long-term survival rates, thus decreasing the amount of revision surgeries and complications. Titanium and its alloys are widely used in biomedical applications because of their good mechanical properties, such as strength and durability, resistance to corrosion and biocompatibility [1]. Titanium however does not promote apatite formation and thus its bone-bonding abilities are less than ideal in physiological environment, and in order to improve the adhesion a wide range of surface modifications have been utilized over the years[1-3].

In addition to mechanical surface modifications a number of biologically active coating materials have been studied to improve the bioactivity of titanium, including bioactive ceramics such as bioglass [4] and hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HA) [5]. The synthetic HA imitates biological calcium-deficient hydroxyapatite found in human body [6], and it has been shown to promote implant integration directly to bone without intermittent connective tissue layer [7-9]. Metallic implants release ions into the surrounding environment which can lead to foreign body reaction and loosening of the implant [10], and it has been suggested that coating with bioactive material can also reduce the metal ion release from implants [11]. The optimal HA coating material should have as high as possible chemical purity ($\geq$ 95%) with Ca/P-ratio close to stoichiometric 1.67 and the microstructure should imitate crystals found in human bone [5, 12]. Coating layer thickness should be controlled, since thick HA layers have typically weaker mechanical properties, and they will smoothen out possible micro-scale modifications made to the substrate surface [5, 13].

Several coating methods have been developed to produce hydroxyapatite coatings on metal implants, e.g. plasma spraying [14, 15], sol-gel technique [16, 17], pulsed laser deposition [15, 18], magnetron sputtering [19] and electrophoretic deposition [20, 21]. Plasma spraying of titanium implants has been studied intensively over the years and there is evidence *in vivo* [9] and from clinical use [7] of its strong osteoconductive properties. Plasma spraying is

suitable for producing cost-effectively coatings with thickness between 30 to 200 μm [2], but plasma sprayed coatings suffer from low cohesive strength [22] and high process temperatures that can cause inhomogeneity of the chemical composition and/or crystal structure [23, 24], and induce cracking of the HA layer. To improve the coating adhesion and crystalline structure there have been studies with post-deposition heat treatments [25], but due to residual stresses caused by different thermal expansion coefficients the annealing can cause crack formation [26] and delamination of the coating in physiological environment [27]. Plasma spraying is also a line-of-sight method [28], which limits its use to simple two-dimensional geometries, and thick coating layers easily mask substrate surface features meant to improve coating adhesion and cell integration [13].

Atomic layer deposition (ALD) is a form of chemical vapor deposition technique that is used for creating highly conformal thin film layers on various substrate materials [29]. ALD is based on self-limiting surface reactions of typically two gaseous precursor chemicals that are supplied sequentially into a reaction chamber, and the final coating thickness can be controlled on atomic level by adjusting the number of reaction cycles [30]. Calcium or calcium-containing thin films, such as calcium oxide (CaO), have been deposited by ALD using $Ca(thd)_2$ (thd=2,2,6,6,-tetramethyl-3,5-heptanedionato) [31] or cyclopentadiene type precursor [32] as calcium source. Different precursor compositions have been studied as phosphorous source, e.g. PH_3 [33], or $(CH_3O)_3PO$ [34]. Putkonen et al. [35] described a method to produce calcium phosphate layer by ALD using a combination of $Ca(thd)_2/O_3$- and $(CH_3O)_3PO/H_2O$-precursors. They succeeded in producing amorphous calcium phosphate thin films in relatively low process temperatures, and they were able to adjust the phosphorous to calcium ratio by carefully controlling the ALD precursor materials' pulsing ratio. However, a high temperature (>500 °C) post-deposition annealing in moist nitrogen was required to crystallize the films to hydroxyapatite.

Holopainen et al. [13] developed a method for manufacturing very thin, uniform layer of nanocrystalline hydroxyapatite from atomic layer deposited calcium carbonate thin film. The calcium carbonate layer was deposited on top of titanium substrate by ALD using $Ca(thd)_2$ and O_3 as precursor materials and converted into hydroxyapatite by immersing the substrate

into pre-heated dilute phosphate solution. The benefits of this method are low process temperatures, superior penetration and coverage of complex three-dimensional shapes, small final coating layer thickness and stability in biological environment. In this paper we continue the development of this coating method and compare the mechanical adhesion of several versions of this nanocrystalline HA coating material to define the most suitable option for implant use. The mechanical properties are evaluated using tensile adhesion and scratching test methods, and we also evaluate the failure methods and interfaces after testing using light and electron microscopy.

2. MATERIALS AND METHODS

2.1 Film preparation

Thin films of calcium carbonate ($CaCO_3$) were deposited in F-120 ALD reactor (ASM Microchemistry Ltd., Finland) under nitrogen atmosphere and approximately 5-10 mbar pressure. High-purity N_2 was used as a carrier and purging gas. Substrate material used for these studies was 50 x 50 x 1 mm^3 unpolished Grade 2 Titanium sheet (William Gregor Ltd., London, UK), meeting the ASTM B265 specifications. For cross-section thickness analyses some films were also grown on silicon. Substrates were cleaned in ultrasonic bath, rinsed with ethanol and blown dry with nitrogen gas prior to deposition.

$Ca(thd)_2$-O_3 ALD process was used to produce calcium carbonate thin films as previously described by Nilsen et al. [30] Ozone gas was generated by feeding pure O_2 (99.9999%) into a Wedeco Ozomatic Modular 4 HC Lab ozone generator, and $Ca(thd)_2$ (Volatec Oy, Finland) was evaporated from an open source boat at 188 °C. Process temperature was 250 °C, and samples were produced with 2000 and 4000 ALD cycles, with resulting calcium carbonate thin film thicknesses of 95 nm and 190 nm.

$CaCO_3$ thin films were converted to nanocrystalline hydroxyapatite by immersing the substrates for 1 min in dilute phosphate solutions preheated to 95 °C. Conversion solutions

were manufactured by dissolving diammonium hydrogen phosphate (DAP, $(NH_4)_2HPO_4$, Merck, 99%) into concentration of 0.2 M in deionized water or 1M NH_3 solution. After treatment, the samples were rinsed with deionized water and blown dry with compressed air.

2.2 **Characterization**

Adhesion of nanocrystalline hydroxyapatite layer on titanium substrate was measured by Positest ATA20 hydraulic adhesion tester (DeFelsko Co., USA) in accordance with ISO 4624 and ISO 16276-1. Test plates (approximate size 25 x 25 x 1 mm^3) were cleaned by sonication in 100 % ethanol for 3 min. Self-aligning aluminium dollies with 10 mm diameter were roughened with sandpaper (P80) and cleaned by sonication in 100 % ethanol for 3 min. Dollies were then glued with an epoxy resin adhesive (Loctite EA9466 or EA9497) to a coated titanium plate and were left to cure in room temperature for minimum of 48 hours. Tests were repeated four times for each sample type, and used pull rate was 1.0 MPa/s.

Scrath testing was carried out according to SFS-EN 13523-12. Scratches were produced using a 10 μm spherical diamond tip with a minimum distance between consecutive scratches at least 4 mm to ensure independent behaviour of each scratch. Two sets of scratches were produced with Instron 3366 on test plates: short scratches (5 mm) with constant loads and longer scratches (40 mm) with step-wise increasing loads. Short scratches were produced with table speed of 0.1 mm/s and the loading increased from 0 N with approximately 15 mN steps between parallel scratches to maximum load of 122 mN. With long scratches the loading was increased in 4 mm intervals starting from 0 N up to highest load of 370 mN with table speed of 0.2 mm/s, and a total of six identical scratch traces were produced on each sample. Tested samples were produced with alkaline conversion solution and either 2000 or 4000 ALD process cycles.

Film crystallinity was examined by X-ray diffraction (XRD) with a PANalytical X'Pert Pro MPD diffractometer using CuKα radiation in grazing incidence geometry and an incident angle of 1°. The hydroxyapatite films as-prepared and after adhesion and scratch testing were characterized with field emission scanning electron microscopy (Hitachi S-4800 and Sigma

HD VP FE-SEM). Some samples were sputter coated with a 4 nm layer of Au/Pd prior to FE-SEM imaging to improve image quality. Film thicknesses were evaluated from FE-SEM cross sections from the edges of unpolished samples cut from of HA films on silicon. Samples were stained after adhesion testing with alizarin red that binds to calcium by preparing 2 % solution of the dye in deionized water, and pH of the solution was adjusted to 5.7 with 1 M NaOH. Samples were immersed in the dye for 10 seconds and the extra dye was rinsed with deionized water and blown dry with compressed air.

2.3 **Statistical analysis**

All quantitative data are expressed as mean ± standard deviation. Differences between means were analysed for statistical significance using Student's t-test for independent samples. Statistical significance was considered at $p < 0.05$. All data were analyzed using IBM SPSS Statistics v. 24.0 software.

3. RESULTS

All of the prepared hydroxyapatite films had a plate-like hydroxyapatite crystal structure as identified with FE-SEM and XRD (Fig. 1). No significant differences were observed in the surface morphology between the films converted from 2000 and 4000 cycle $CaCO_3$ films, nor between the films converted with basic and neutral solutions similarly to what was previously reported in the initial study by Holopainen et al [13]. Cross-section thickness analyses of the coatings revealed that even though the calcium carbonate thin film thickness increases linearly based on the number of ALD process cycles, this behaviour changes in the conversion in phosphate solution to hydroxyapatite. After conversion the thin film thicknesses were approximately 300 nm (2000 cycles) and 380 nm (4000 cycles) indicating that some densification is happening in the thicker coating layer compared to the thinner film during the conversion process (Fig. 2).

3.1 **Adhesion testing**

The results for the adhesion tests are presented in Fig. 3, and based on these results it can be seen that adhesion values are higher with alkaline conversion solution and 4000 ALD cycles compared to adhesion with neutral conversion solution ($p = 0.005$ for 2000 cycles DAP, $p = 0.009$ for 4000 cycles DAP). Increasing the cycle amount from 2000 cycles to 4000 cycles seems to also improve the adhesion ($p = 0.001$) when using alkaline conversion solution. Holopainen et al. also reported that post-conversion annealing improves the adhesion of the coating layer [13], but in current results the difference between annealed and non-annealed coatings is only 0.8 MPa in favour of the annealed coating but the difference is not statistically significant ($p = 0.39$).

Analysis of the samples with FE-SEM revealed that the hydroxyapatite crystals were intact in the adhesion test area after testing in the samples with the highest measured tensile strength, i.e. samples produced with 4000 cycles and alkaline conversion solution. This indicates that the failure mode in these samples was cohesive and the results correlate more with the glue adhesion strength (EA 9466) than with the actual coating adhesion to substrate material. Samples prepared for adhesion testing with EA 9497 glue performed inferiorly in testing, but further inspection with light and electron microscopy revealed that the samples were covered with a thin glue layer after testing, leaving the hydroxyapatite layer underneath intact. After heat treatment we couldn't find any microcracks or other damage to the coating layer, which have been indicated in some earlier studies with heat treatment of HA coatings [14, 26].

After adhesion testing the samples were stained with alizarin red and the stained samples were photographed and surface areas for cohesive and adhesive failure modes were calculated from the pictures. For the annealed samples the surface area analysis was done with non-stained samples under light microscope. Adhesive failure relates to a situation where the coating is detached from the titanium surface, and cohesive failure occurs either inside the coating layer or at the interface between the coating and the glue layer. Mixed failure mode can be defined as a combination of adhesive and cohesive failures, and it has been found that in some previous studies that it is a quite typical failure mode for this testing method [36, 37] . In the

stained samples the uncoated titanium surface does not stain with alizarin red, the calcium of the remaining HA layer has red or light green appearance and glue layer stains purple in the process (Fig. 4). The structure of the red and light green areas were also inspected with FE-SEM, where light green areas were confirmed to contain intact nanocrystalline HA structure. The adhesion results have been compiled with failure mode in Fig. 5, and it can be concluded from the results that the measured adhesion strength correlates with adhesive failure portion in such a way that when the adhesive failure mode dominates the measured adhesion values are lower. Similarly, with cohesive failure mode dominating the adhesion values are higher, except for the EA9497 glue samples in which the glue layer the detachment had happened inside the glue layer (low adhesion strength). These findings support the conclusion that with adhesive failure mode samples the separation is happening in the coating-substrate interface and with cohesive failure modes the detachment is happening either inside the coating layer or in the glue-coating interface.

3.2 **Scratch testing**

Macroscopic plastic deformation of the coating produced with alkaline conversion solution and 4000 ALD cycles seemed apparent in scratch testing with the lowest testing force used (14 mN), but it appears from the FESEM pictures that the scratching tip is actually pushing the coating material in front of and under the scratching tip rather than revealing the titanium base material (Fig. 6). This suggests that the coating material has modest cohesive strength, but does not give additional information about the adhesion between the HA and the titanium. As the scratching force increases to 67 mN the groove gets markedly deeper and the width of the groove converges with the width of the scratching tip. Same phenomenon can be seen with samples stained with alizarin red, where with smaller stresses red calcium-containing material is still visible in the groove, but as the force increases to 67 mN pure titanium is revealed in the bottom of the groove (Fig. 7c&d). In the samples produced with 2000 cycles this HA delamination can be detected already with a loading level of 40 mN (Fig. 7a&b), and when observing these samples with FESEM it appears that the scratching grooves are shallower and narrower than in the samples produced with 4000 cycles. Scratching test

results thus appear to be in accordance with adhesion test results, indicating that the thicker coating layer is superior in adhesion to the titanium substrate compared to thinner coating.

4. DISCUSSION

Ensuring proper adhesion to the implantation site and promoting integration with bone cells are key focus areas in improving the long-term survival of the titanium implants in medical use [38]. Modifying the implant surface by using biologically active coating materials [39], such as bioactive glass [40] or hydroxyapatite [14], has proven to be one of the most promising ways to improve the osseointegration of the implant. Bioactive coatings can be also used to protect the substrate surface [10, 11] from physiological environment as well as wearing or damaging of the surface in the assembly phase and in long-term use, thus leading to lower amount of metal ions released into the surrounding tissues [41].

In this paper we have studied the mechanical properties of a nanocrystalline hydroxyapatite coating converted from atomic layer deposited calcium carbonate thin film, resulting in highly conformal and uniform coating layer that can be applied on complex three dimensional structures. Relatively low process temperatures compared to other manufacturing methods help to reduce residual stresses and cracking of the coating layer. With a final coating thickness of less than 400nm the surface features aimed for better cell attraction and adhesion are not covered by the coating layer, which can be an issue with other thicker HA coating methods such as plasma spraying. Thickness of the ALD calcium carbonate thin film can be controlled by adjusting the number of ALD cycles, but after conversion to nanocrystalline HA the final coating thickness does not increase linearly, likely due to densification of the coating layer in the conversion phase.

Using adhesion and scratch testing we defined the best process parameter combination for this coating solution, and highest adhesion values were acquired with coating that was produced by 4000 ALD cycles and converted to hydroxyapatite in alkaline solution. Post-conversion annealing at 700°C for 30 minutes improved the adhesion test results by 0.8 MPa compared

to non-annealed samples, but the difference was not statistically significant. Based on these measurements the adhesion of ALD HA coating (highest value 6.71 MPa) seems to be lower than reported values for the most widely used plasma sprayed HA coatings (ranging from 10 to 60 MPa in different studies [36, 42]). Measurement results are affected by the gluing process parameters such as the amount of glue used, the flatness and cleanliness of the surfaces as well as the surface roughness of the dolly interface, room temperature and relative humidity in the sample preparation area etc. Pretreating the substrate surface before coating with sandblasting, acid-etching or similar methods, could improve the adhesion of the HA coating to the titanium surface significantly [43].

However, further examination of the samples under FE-SEM revealed that the hydroxyapatite crystals were intact in the adhesion test area depending on the sample type, and the amount of observed damage correlated with the failure mode. Crystals were undamaged in the samples with dominantly cohesive failure mode, i.e. samples that were produced with 4000 cycles and alkaline conversion solution, and the damage to the hydroxyapatite layer increased with higher adhesive failure percentages. This is in accordance with the previous findings [36, 37] that the adhesion values in pull-out testing represent the bonding strength of both interfaces (between the coating and the substrate and between the coating and the glue) as well as the cohesive strength of the coating and the glue layers. The real adhesion values between the coating and the substrate could thus be higher than what was now measured, which brings into consideration the challenges with current adhesion testing methods [44, 45], and the need to further develop these measurement methods for improving the reliability and comparability of the results [46].

Scratch testing situation compares better to surgical assembly situation and long-term usage wearing conditions, and we find it noteworthy that the coating material seems to first deform under loading and only after increasing the load the coating starts to peel off from the surface. This would indicate that some amount of damage could be tolerated to the coating layer in the assembly phase, which is highly likely to happen in an implant operation.

Considering the implant long-term functionality in physiological environment it could be reasonable to further improve this HA ALD coating method by optimizing the process

parameters and/or studying the effect of various titanium pre-treatments, such as sandblasting or acid-etching, to the adhesion of the hydroxyapatite coating. Also, further studies are needed to analyze the performance of the HA coating in cell culturing conditions and with human osteoblasts and osteoclasts *in vitro*.

5. CONCLUSIONS

We have shown in this present study that good adhesion can be achieved between the titanium surface and nanocrystalline HA coating produced from ALD manufactured calcium carbonate thin layer. Highest adhesion values were achieved with post-conversion heat treatment in 700 °C for 30 min, with alkaline conversion solution and with higher number of ALD process cycles. Further studies are still suggested to further improve the coating method and to study the adhesion and functionality *in vitro*.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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FIGURE CAPTIONS

Fig. 1 a) Top view of nanocrystalline HA on titanium converted from a 4000 cycle film with an alkaline conversion solution and b) the XRD pattern of a HA film on silicon. The peaks of HA (JCPDS no. 09-0432) are represented in the line pattern.

Fig. 2 FESEM cross-sections of HA films on silicon converted from a) 2000 and b) 4000 cycles films with an alkaline conversion solution

Fig. 3 Adhesion test results with standard errors according to sample type. DAP = neutral conversion solution, NH3 = alkaline conversion solution, * indicates $p < 0.01$

Fig. 4 Adhesion test samples stained with alizarin red, failure surface types marked in the picture: pure titanium (white triangle), glue (white arrow), hydroxyapatite (black square). Red and light green HA areas confirmed with FESEM marked to the picture. HA films converted from 4000 cycle films with (a) alkaline conversion solution, (b) neutral conversion solution

Fig. 5 Adhesion strength and proportion of adhesive failure by sample type

Fig. 6: FESEM picture of scratching tip groove, loads a) 14 mN and b) 67 mN, 4000 cycles, alkaline conversion solution

Fig. 7: Scratching test samples stained with alizarin red, alkaline conversion solution, a & b 2000 cycles, c & d 4000 cycles. Base material revealed with a) 40mN and b) 67 mN loading (➤)

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Fig. 1

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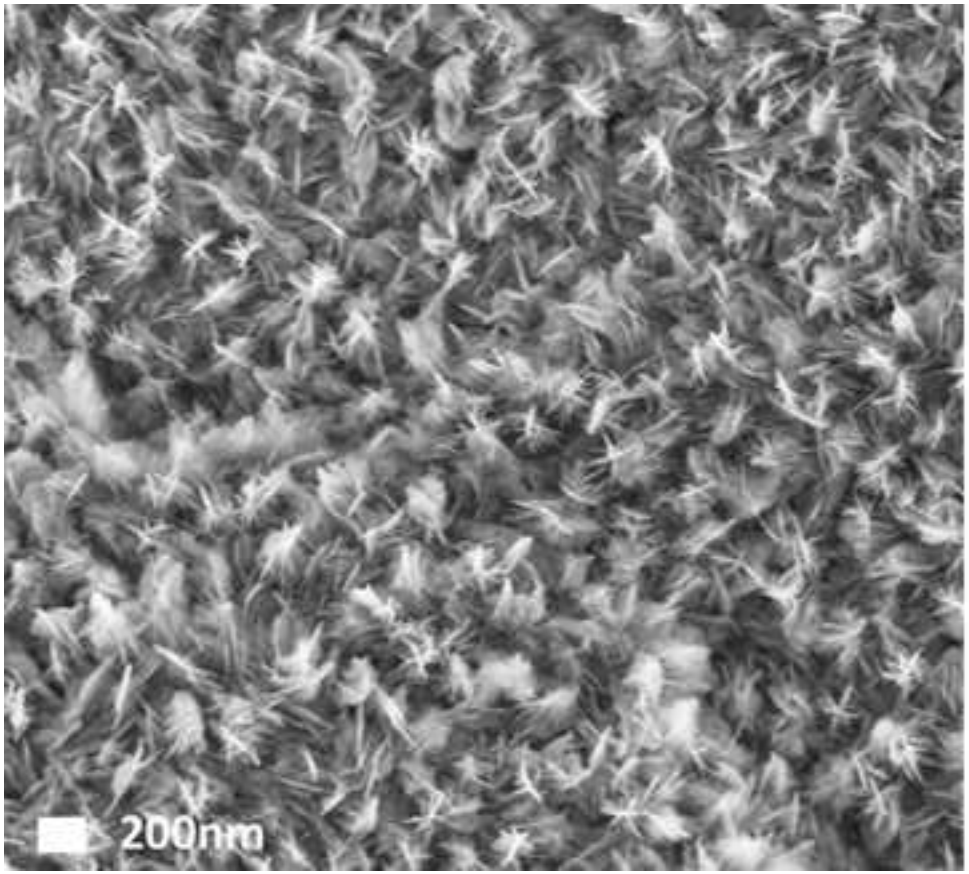

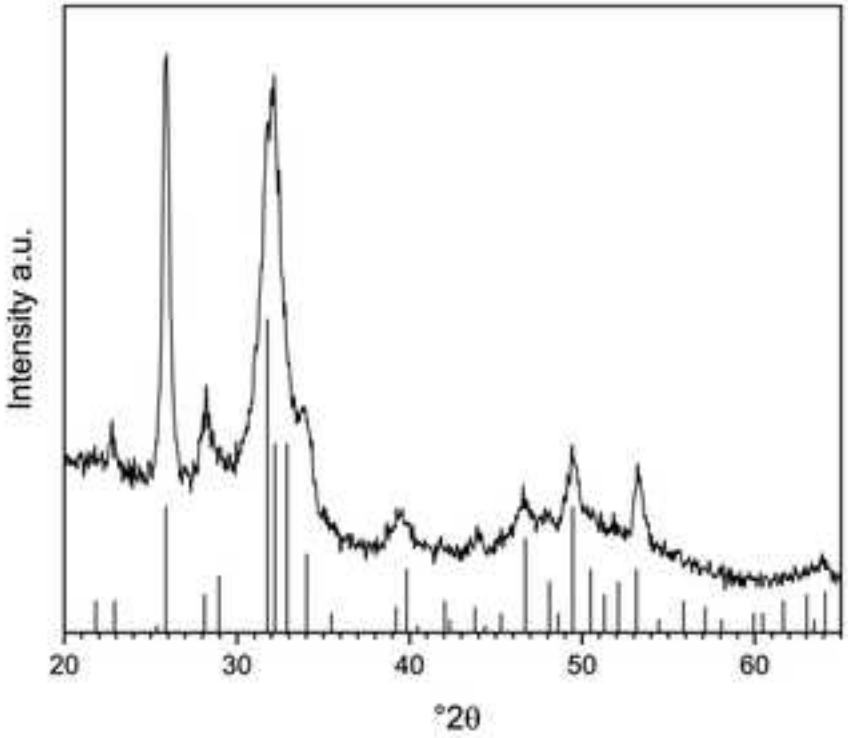

Fig. 2

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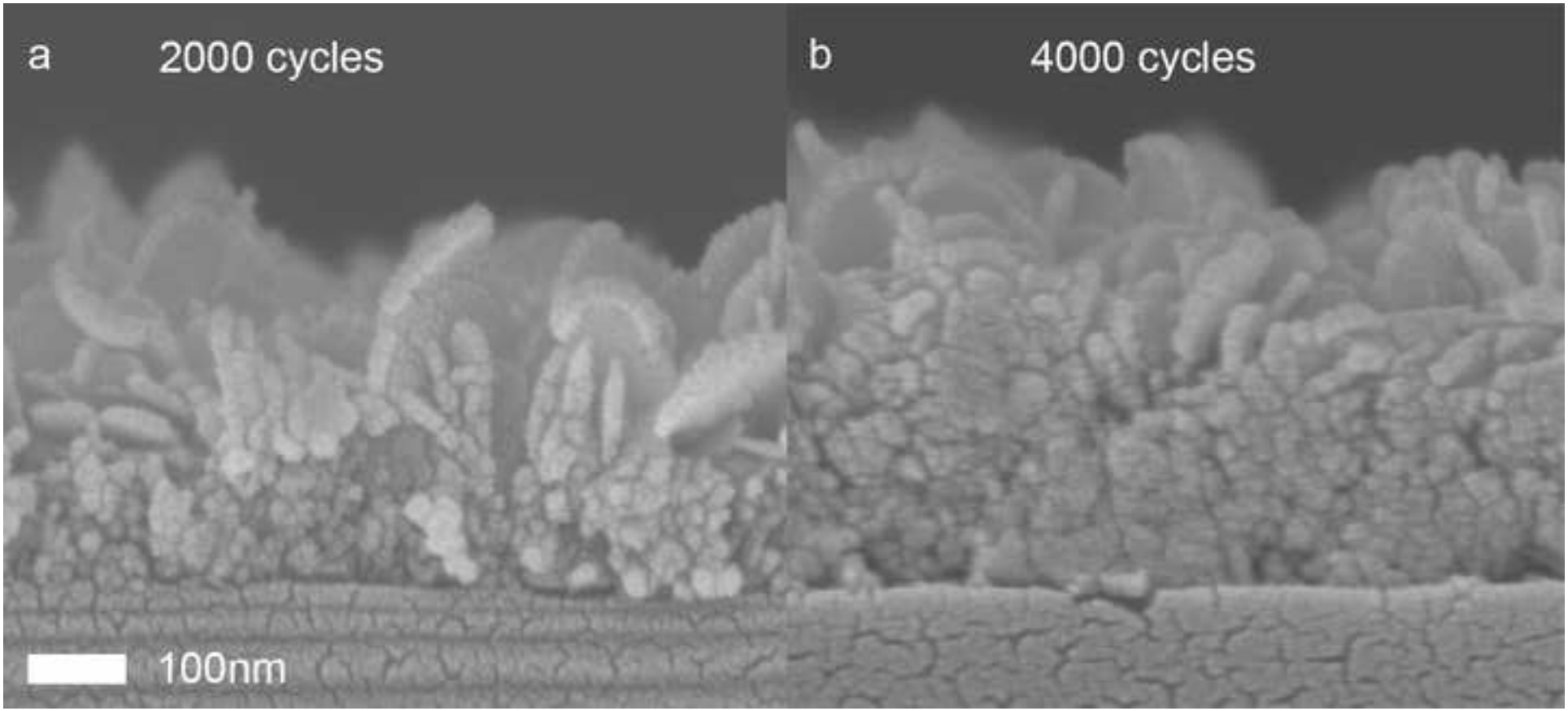

Fig. 3

Click here to download Figure Fig3.tif

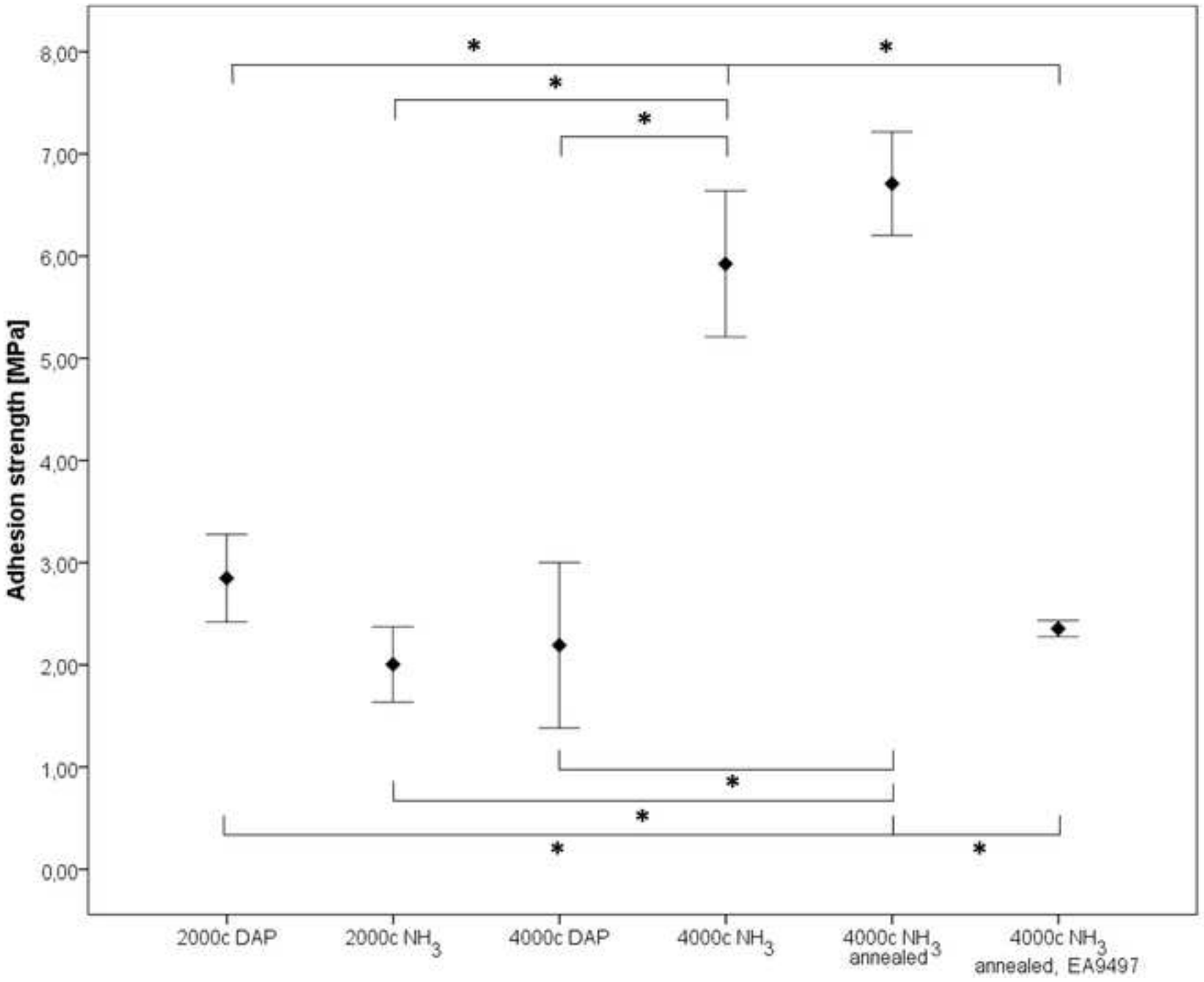

Fig. 4

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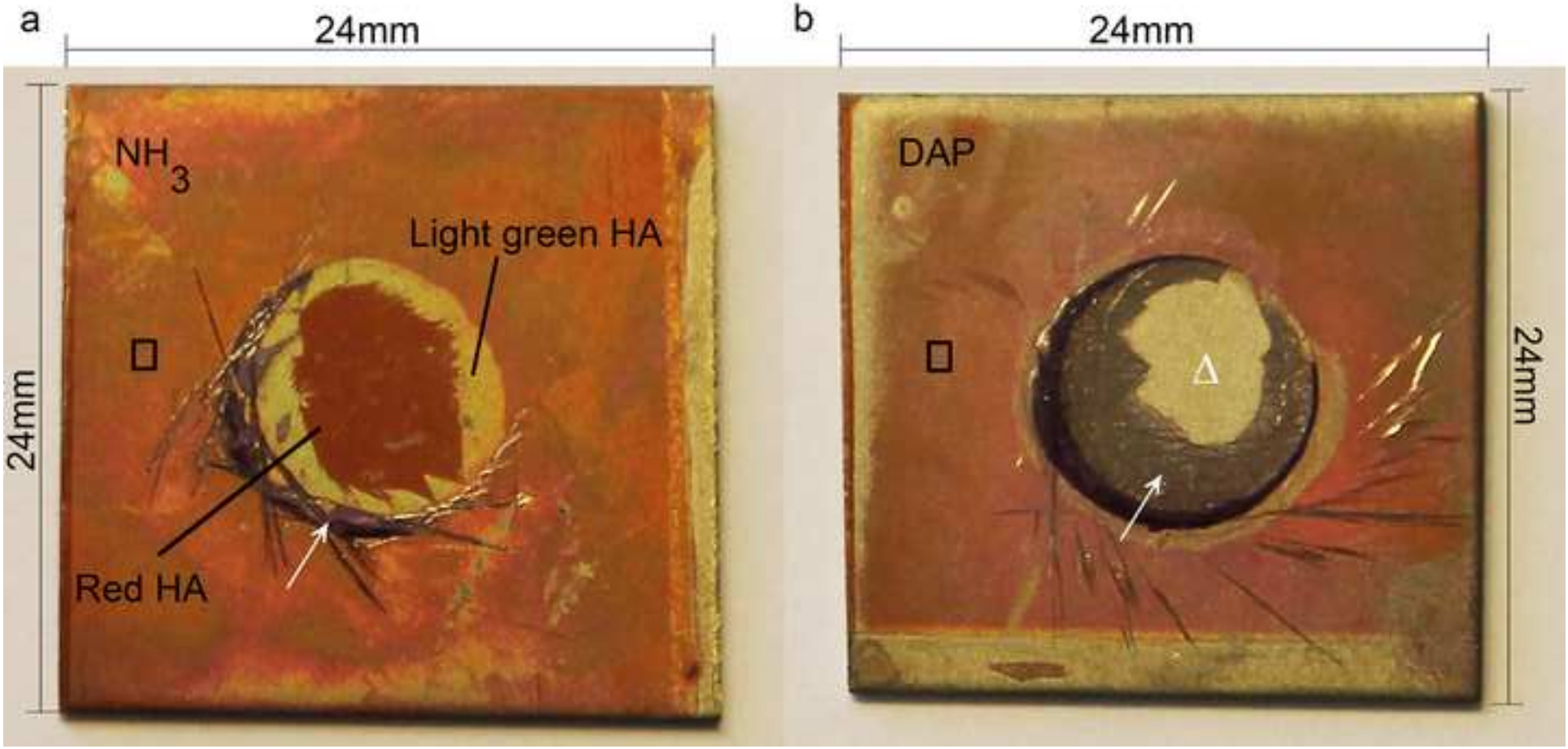

Fig. 5

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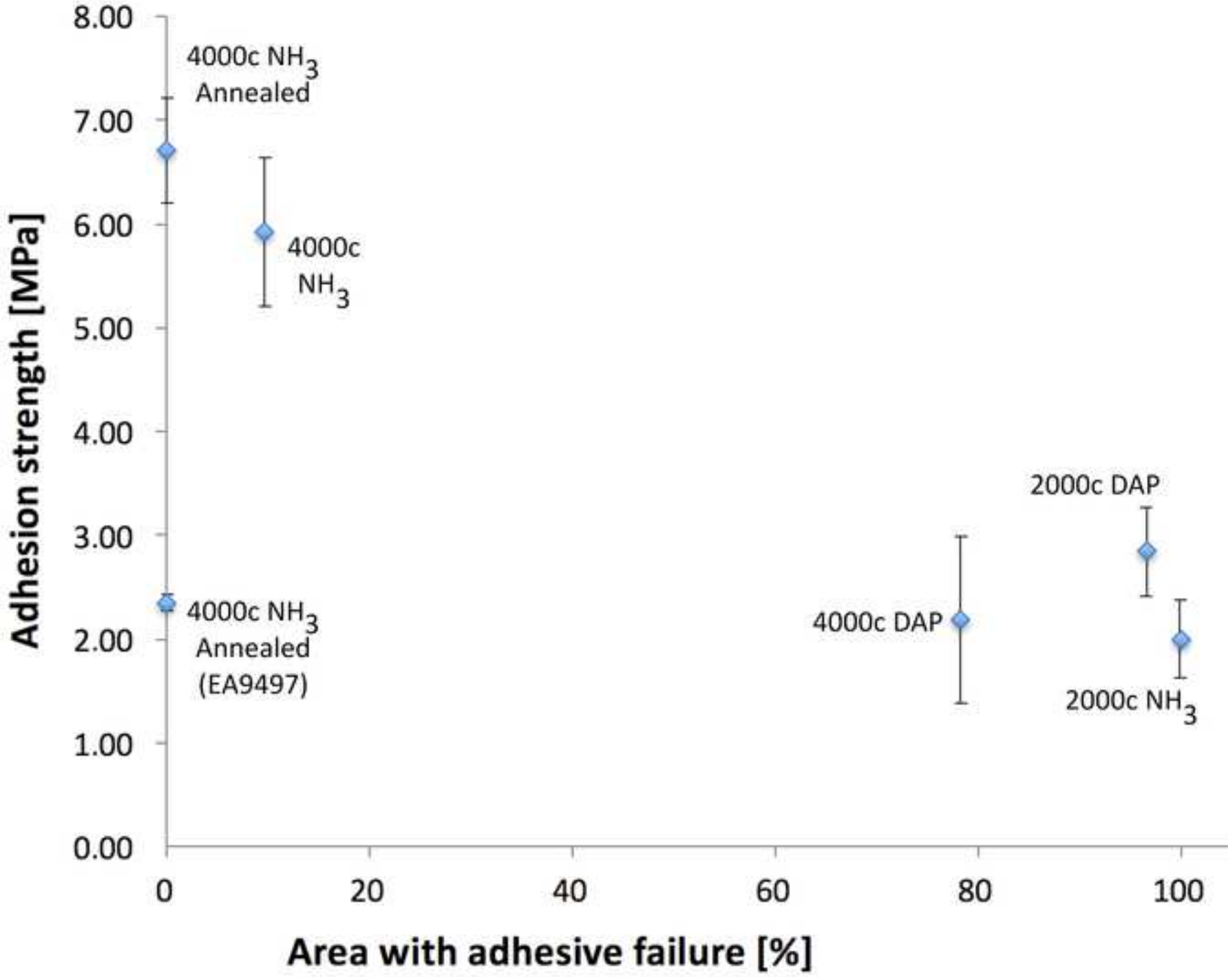

Fig. 6

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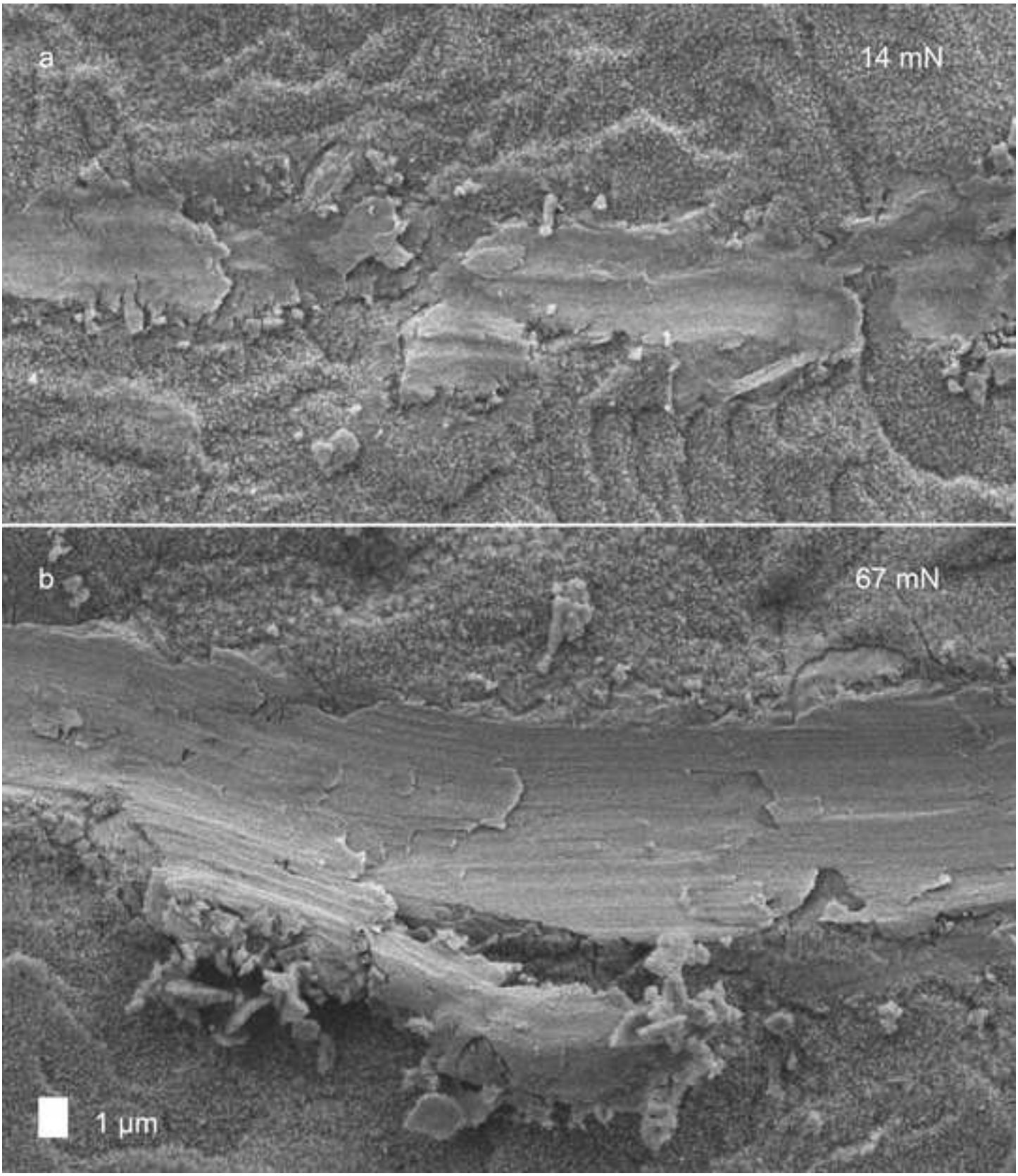
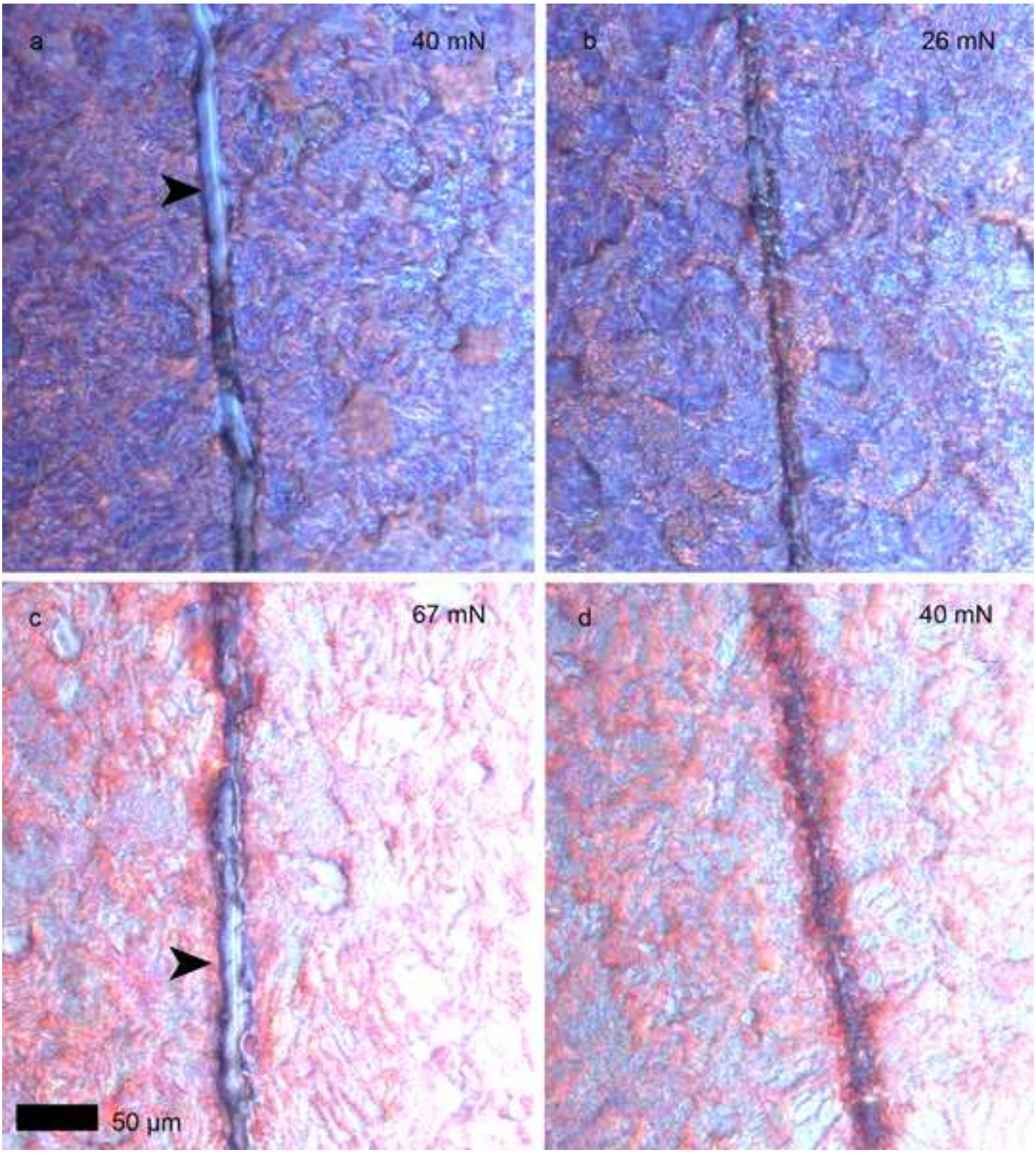


Fig. 7

Click here to download Figure Fig7.tif



Graphical Abstract