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Subcutaneous tissue response to titanium, poly(ε-caprolactone), and carbonate-substituted hydroxyapatite-coated poly(ε-caprolactone) plates: A rabbit study

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Abstract: The aim of this study was to evaluate the soft tissue response to poly(ε-caprolactone) (PCL) implants with and without carbonate-substituted hydroxyapatite (CHA) coating compared to the commonly used titanium alloy (Ti-6Al-4V)-machined surface. Experimental materials were implanted subcutaneously in New Zealand white rabbits for 5 weeks. The tissue attachment strength, as evaluated by a tissue peel test, histological and histomorphology analysis, as well as scanning electron microscopy were compared between groups. The peel test result revealed no statistically significant difference between groups. Histological analysis found fibrous capsule formation around all implant materials. The fibrous capsule around PCL implants with and without CHA coating was significantly thinner compared with the capsule thickness around the titanium implants. However, the inflammatory cells, as present at the fibrous capsule-implant interface, were found to be significantly lower in **the** Ti-group. In conclusion, the current data do not prove that PCL or PCL with a CHA coating results in a superior soft tissue response compared with a machined titanium implant. © 2013 Wiley Periodicals, Inc. J Biomed Mater Res Part A: 101A: 2258–2266, 2013.

Key Words: poly(ε-caprolactone) (PCL), carbonate-substituted hydroxyapatite (CHA), tissue response, tissue peel test

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INTRODUCTION

In previous studies, a titanium modular mandibular endoprosthesis has been developed to repair segmental defects of the mandible, which demonstrated stability and good fixation to bone in animal studies.[1,2] However, in some instances, dehiscence has proven to be a problem especially when the soft tissue does not adhere to the body of device, with subsequent exposure of the prosthesis.[3]

It is known that implant surface chemistry, shape, and mechanical properties are all factors that affect the implant-soft tissue adhesion.[3] For example, implant surface topography has a major effect on implant tissue response.[4] Smooth-surfaced implants result in a foreign body reaction, which is characterized by fibrous tissue encapsulation of the implant and the presence of inflammatory cells at the implant–soft tissue interface. On the other hand, implant surface roughness can have a favorable effect on the soft tissue response. It has been suggested that implants with a surface roughness value of 3.3 microns or larger tend to become infiltrated with inflammatory tissue, while implants with a surface roughness value 1 to 2 microns porosity appear to allow direct fibroblast attachment to the surface, which is supposed to be independent of the physico-chemical nature of the implant surface.[4] Although the relationship between material surface topography and cellular behavior is complex and still not fully understood, Unadkat et al. hypothesized that changes in the surface topography can affect cellular responses to a material by mimicking the influence and action of growth factors.[5] Substrate surface features have been shown to induce significant modulation of focal adhesion formation, cytoskeletal development, and cellular spreading, changes that are subsequently transduced to signaling pathways, affecting functional differentiation through integrin-specific signaling pathways.[6] Surface roughness and total surface area of an implant can be favorable for increased cell adhesion and migration as well as the

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production of extracellular matrix (ECM). In view of this, implant surfaces with a texture such as nodes, pores, grooves, or random patterns are often associated with a marked change of cell morphology, cell activity, and cellular production of autocrine as well as paracrine regulatory factors compared to the smooth surface.[7]

Implant surface roughness can be created by adding or subtracting material from the implant surface. The addition of material can be done by a coating procedure,[8,9] that is titanium plasma spraying, and subtraction can be done by grit-blasting [10–12] or etching procedures.[13,14] Most of the studies to date have investigated the effect of increased surface roughness of the implant on bone regeneration. However, less studies have investigated the effect of increased surface roughness of the implant on soft tissue attachment. Lee et al. designed an experiment to study the effect of titanium surface modification on soft tissue attachment.[3] Both machined surface and -etched titanium bullets were implanted for 6 months in the muscle of *Macaca fascicularis* monkeys. The histological results showed a lack of direct contact between muscle tissue and machined titanium implant surface. Also, surface etching did not result in a significant improvement to the soft tissue attachment compared to the machined titanium surface.[3]

Although titanium is preferred for bone reconstruction due to its mechanical strength and ability to withstand long-term loading, tissue adaptation to the titanium surface is still limited. The soft tissue response to an implant material is also dependent on the mechanical properties of the biomaterial.[15] In general, less stiff biomaterials improve the soft tissue response. The mechanical properties of polymers are easier to fine-tune to get a better soft tissue response than metals, like titanium. A candidate material, as can be used for the fabricating of a modular endoprothesis with an improved soft tissue adaptation, is poly(ε-caprolactone) (PCL). This material has several advantages over other polymers. It is more stable in ambient conditions, significantly less expensive, and is readily available in large quantities.[16,17] In addition, PCL can be easily combined with other materials to further formulate the tissue response. Active screen plasma surface modification has been shown to improve osteoblast cell adhesion and spreading on the PCL surface[18], while chemical hydrolysis to introduce carboxylate groups onto the surface of the PCL was found to improve surface wettability and roughness of the PCL, which was correlated with increased cell attachment.[19] Several techniques are available to manufacture an implant from PCL. One of the approaches is laser sintering, where small PCL particles are selectively fused layer by layer by a high-power laser to build a three-dimensional (3D) device. This method allows adaptation of the mechanical properties of the final implant.[20] Selective laser-sintered (SLS) and solid free-form fabrication (SFF) manufactured PCL scaffolds with a porosity between 37 and 55% were reported to have mechanical properties comparable with human trabecular bone. The compressive modulus of such scaffolds was found to be within the 52–68 MPa range, and the ultimate compressive strength was within the 2.0–3.2 MPa range, which makes this material an attractive substitute for human bone and its application for bone reconstruction in load-bearing areas.[20]

For the current study, we hypothesized that implants made of PCL would lead to better soft tissue adaptability and adhesion than commercially pure titanium implants. In addition, we supposed that surface roughening, created by the deposition of a carbonate-substituted hydroxyapatite (CHA) coating on PCL, would further improve the soft tissue response. Therefore, implants were incubated in modified simulated body fluid (mSBF), which resulted in the nucleation and growth of a CHA coating on the implant surface.

A subcutaneous rabbit model was used to study the soft tissue response. Analysis after 5 weeks of implantation was based on a tissue peel test to determine the force required to separate the soft tissue from the various implant surfaces and on light microscopy examination.

MATERIALS AND METHODS

Implant materials

Non-coated PCL, CHA-coated PCL, and commercially titanium (Ti) implants were manufactured. The implants were rectangular-shaped, measured 10 × 5 × 3 mm, and were provided with rounded off corners and edges. The PCL implants were fabricated via laser sintering as previously reported.[20] The PCL implants were used as-received or were coated with CHA by incubation at 37°C in mSBF for 8 days under continuous rotation. Prior to mSBF incubation, the PCL plates were hydrolyzed in a 1 M NaOH for 60 min. After hydrolysis, plates were rinsed and incubated in the mSBF. The mSBF solution has a similar composition to that of human plasma and also to that of the SBF solution reported by Kokubo et al., but with double the concentration of calcium and phosphate to enhance mineral growth, and was prepared as previously reported.[21,22] Briefly, 141 mM NaCl, 4.0 mM KCl, 0.5 Mg SO_4, 1.0 mN $MgCl_2$, 4.2 mM $NaHCO_3$, 5.0 mM $CaCl_2$, and 2.0 mM KH_2PO_4 were dissolved in deionized ultra-filtered water, pH was adjusted to 6.8 with 2N HCl or 2N NaOH.

Prior to their use in the *in vivo* study, PCL and CHA-coated PCL implants were sterilized by ethylene oxide, and Ti-plates were sterilized by autoclave.

Animal model and implantation procedure

The animal experimental protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of Singhealth, Singapore. The animal laboratory was certified by the International Association for Assessment of Laboratory Animal Care (IAALAC).

Nine female New Zealand white rabbits, 3–4 months old, were used in this study. The surgery was performed under general anesthesia by intramuscular injection of 1.5 mg Ketamine (Parnell Laboratories, Alexandria, Australia). Anesthesia was maintained by 1-1.5% isoflurane gas through a mask with constant volume ventilator. Heart rate and oxygen saturation were monitored during the procedure.

Prior to surgery, the skin was shaved, washed, and disinfected with povidone iodine 1% solution, Hexodane 0.5%

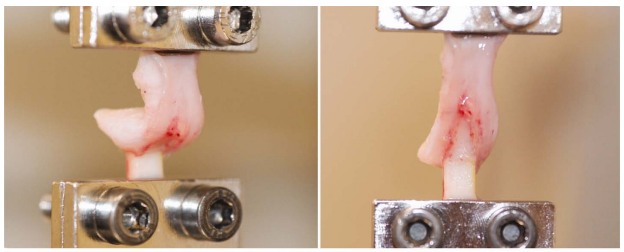

FIGURE 1. Specimens were installed in Instron® 8800 machine for tissue peel test: (a) before and (b) during peel test for the PCL plate. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

(Chlorhexidine 0.05% W/V in Methylated Spirit 70%), and centrimide 1% solution. Each animal was given a unique code. Six longitudinal incisions of about 1.5 cm were made at the left and right side of the vertebral column at 3 cm apart from each other. Six subcutaneous pockets were prepared by blunt dissection with scissors. Each of the pockets in each animal received one of the three types of implants. A randomization schedule was made for implant allocation, which listed the animal's code and the corresponding subcutaneous pocket number (1–6) in each animal.

Six implants (two PCL, two CHA-coated PCL, and two Ti) were inserted into each rabbit. With nine rabbits used, a total of fifty-four implants were inserted (18 PCL, 18 CHA-coated PCL, and 18 Ti). After implant installation, the wounds were closed using 3-0 Vicryl® intracutaneous sutures (Ethicon, Somerville, NJ). After 5 weeks, all animals were euthanized, and the implants with surrounding tissues (a rectangular patch of the skin encompassing each plate) were harvested.

After harvesting, the retrieved specimens were divided into two equal-sized groups, that is, one group was used for testing of the soft tissue adhesion strength, and the other was used for histological analysis.

Peel-test procedure

Immediately after harvesting of the plates, 27 samples (nine of each plate type) were subjected to a soft tissue peel-test using an Instron® 8800 microforce tester (Instron Corporation, Satec™, Norwood, MA) equipped with a static load cell with a capacity of 10 N.

All specimens were prepared before installation into the Instron® machine (Fig. 1), that is, one-third of the plate surface was exposed to allow its grip by the lower grip of the machine, while the remaining two-thirds of the attached tissue was kept intact to the plate for the peel test. One end of the soft tissue was attached vertically to the upper grip of the testing machine, and the plate surface was kept parallel (180 degree) to the tension force. A tension force was applied with the top upper arm of the machine, which was moving upwards at a speed of 5 mm/min. The test was carried out until tissue was completely peeled off from the plate surface. Mechanical data were recorded, and the corresponding force–displacement curves were generated. The values of maximum force attained were then averaged, and the standard deviations were calculated. After performance of the peel test, the specimens were fixed in 10% formaldehyde for further evaluation with scanning electron microscopy (SEM).

Scanning electron microscopy

The morphology of the plates before and after implantation was investigated by SEM. PCL and CHA-coated PCL plates were mounted on aluminum stubs and sputter coated with a thin layer of gold. Samples were imaged under high vacuum using a Philips XL30 FEG scanning electron microscope (Hillsboro, Oregon) operating at 10 kV. Ti-plates were mounted on stub and examined at 20 kV without gold sputter coated.

Histological analysis

Before histological preparation, the specimens with their surrounding tissues were immersed for 1 week in buffered 10% formalin solution for fixation (ICM Pharma Pte, Singapore), and then dehydrated in a graded series of alcohol and embedded in methylmetacrylate. After polymerization, the tissue blocks were mounted in a modified inner circular saw microtome (Leica® RM 2165, Wetzlar, Germany). At least, three histological sections were made from each specimen. Sections had a thickness of 10–15 μm and were stained with methylene blue/basic fuchsin and examined using a light microscope (Olympus® U-D03, Tokyo, Japan).

All sections were observed and independently scored by two blinded observers (N Chanchareonsook and Lee S) using an established soft tissue histology grading scale,[23] as shown in Table I. When the two observers disagreed on a score, the section was discussed until a consensus was reached. The thickness of capsule around implants was measured in micrometers (μm) using 'Cell^{A}' digital imaging software program (Olympus®, Germany). Subsequently, the means of capsule thickness of each implant type were calculated.

Statistical analysis

Data from the peel test and histological measurements were statistically analyzed using SAS 9.2 statistical software (SAS Institute, Cary, North Carolina). Measurements were evaluated by analysis of variance with pair-wise comparison post test to identify the groups that differed from each other. This was done with no correction for the Type I error rate across the pair-wise tests. A p value < 0.05 was considered significant.

RESULTS

Clinical examination

At 5 weeks after surgery, all rabbits tolerated the implant installation very well. Tissue necrosis was observed in only one animal in the area where ketamine was injected. This site was close to a CHA-coated PCL plate. Therefore, this specimen was subsequently excluded from further analysis to avoid an effect on the experimental results. In all other

TABLE I. Soft Tissue Histologic Grading Scale (adapted and modified by Jansen et al., 1994)

Evaluation	Response	Score
Capsule qualitatively	Capsule is fibrous, mature, not dense, resembling connective or fat tissue in the non-injured regions	4
	Capsule tissue is fibrous but immature, showing fibroblasts and little collagen	3
	Capsule tissue granulous and dense, containing both fibroblasts and many inflammatory cells	2
	Capsule consists of masses of inflammatory cells with little or no signs of connective tissue organization	1
	Cannot be evaluated because of infection or other factors not necessarily related to the material	0
Interface qualitatively	Fibroblasts contact the implant surface without the presence of macrophages or leucocytes	4
	Scattered foci of macrophages and leucocytes are present	3
	One layer of macrophages and leucocytes are present	2
	Multiple layers of macrophages and leucocytes are present	1
	Cannot be evaluated because of infection or other factors not necessarily related to the material	0

animals, the surgical sites presented good healing without any wound dehiscence. All plates were palpable through the skin. It appeared that some of the plates had migrated from the insertion site. The Ti-plates had migrated over a distance of 0–4 cm, while CHA-coated and non-coated PCL plates had migrated by 0–1 cm.

Peel testing

Two of the 27 samples were excluded from the peel-test study. One CHA-coated PCL was excluded due to necrosis of skin from the effect of ketamine injection, and one Ti-plate sample was excluded due to formation of hematoma on the plate surface during tissue manipulation at tissue harvesting.

The average energy used for the peel test for Ti, PCL, and CHA-coated PCL was 0.728×10^{-3}, 0.543×10^{-3}, and 0.274×10^{-3} J, respectively. The average peel force for Ti, PCL, and CHA-coated PCL was 0.17, 0.104, and 0.098 N, respectively (Fig. 2).

Statistical analysis of the data showed no significant difference between the mean peak of peel force and energy of peeling between the three experimental materials.

Surface morphology

It is shown from SEM images that the non-coated PCL implants have rougher surface appearance than those of the Ti-implants. The CHA coating, as deposited on the PCL implants, had a microscale plate-like morphology and increased the surface roughness of the PCL implants compared with the non-coated ones. After 5 weeks of implantation, the surfaces of the implants after the peel test were not altered considerably compared to images before implantation (Fig. 3). There were no remaining tissue and cells visible on all plate types after the peel test.

Histological analysis

Evaluation of the histological sections revealed a fairly uniform tissue response for the three types of implant. In all sections, normal skin and underlying tissues, including fat tissue, could be observed. The surface of both CHA-coated and non-coated PCL plates appeared to be rougher compared with those of the Ti-implants. The CHA layer on the coated PCL implants could easily be identified, and a thin red layer on the outer surface of these implants was visible.

All implants were found to be surrounded by a fibrous tissue capsule. This capsule was ~7-8 cell layers in thickness for PCL and CHA-coated PCL implants and 14-17 cell layers for Ti-implants. The capsule had an aligned morphology with collagen bundles running parallel to the

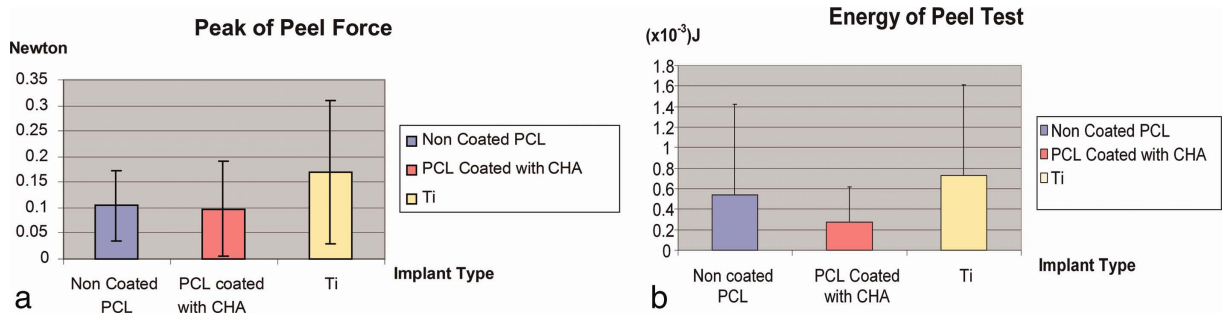

FIGURE 2. Peel test analysis of machined surface Ti-implant, non-coated PCL implant, and PCL surface coated with carbonate-substituted hydroxyapatite (CHA). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

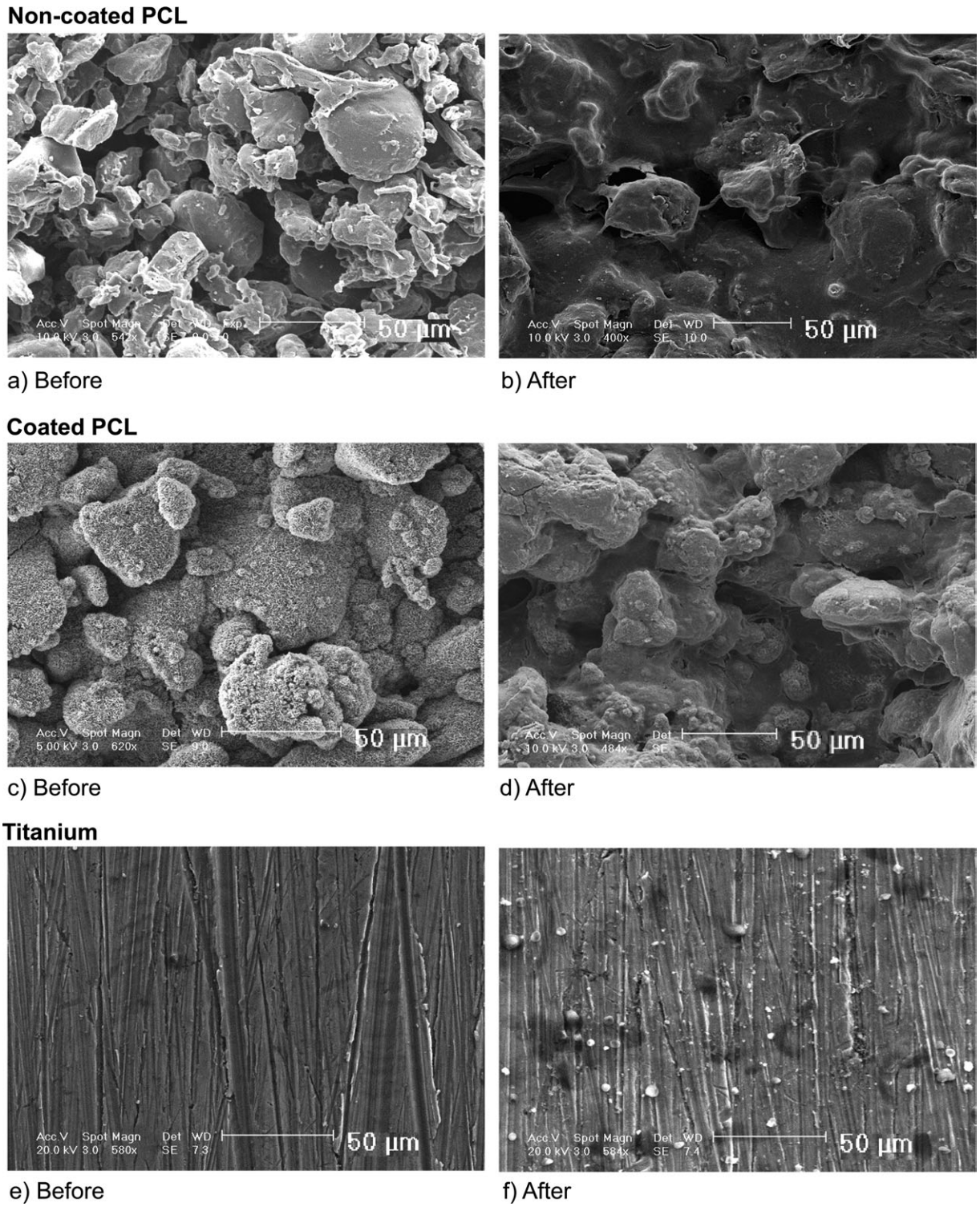

FIGURE 3. Scanning electron microscopy (SEM) images of Ti-plates, coated, and non-coated PCL plates before and after 5 weeks of subcutaneous tissue implantation in the rabbit model: (a) non-coated PCL before surgery, (b) non-coated PCL after implantation and peel test, (c) coated PCL before surgery, (d) coated PCL after implantation and peel test, (e) machined-surface titanium plate before surgery, and (f) machined-surface titanium plate after implantation and peel test. The images demonstrated the rough surface of each implant type, that is, the excellent pattern of microscale plate-like morphology of coated PCL as well as the machined surface appearance of the Ti-plates. The implant surfaces in all type did not show any remnant of connective tissue as left on the surface.

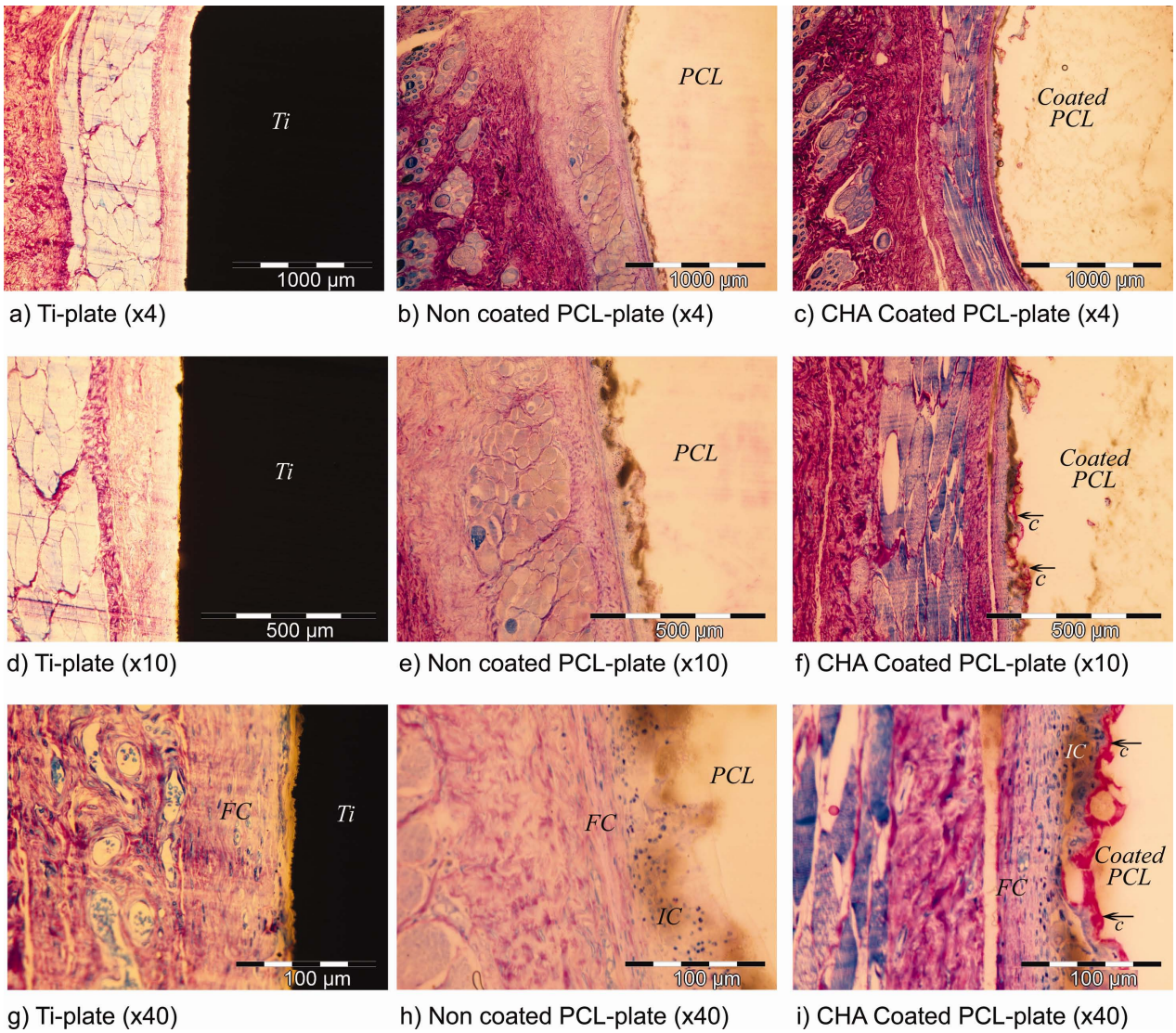

FIGURE 4. Histological images of non-coated PCL plates, coated PCL plates, and Ti-plates after 5 weeks of subcutaneous tissue implantation in the rabbit model Ti: titanium implant; FC: fibrous capsule; PCL: polycaprolactone implant; C: carbonate-substituted hydroxyapatite (CHA) coating; IC: inflammatory cells (methylene blue and basic fuchin). (a) to (c) magnification of ×4, (d) to (f) magnification of ×10, and (g) to (i) magnification of ×40. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

implant surface. Occasionally inflammatory cells were seen in the interface between the capsule and implant surface. The presence of inflammatory cells was more evident for the PCL implants compared with the titanium implants (Fig. 4).

Histomorphometry

The average capsule thickness around the PCL implant was 34.3 ± 15.5 µm, around CHA-coated PCL 50.8 ± 16.4 µm, and around the Ti-plate was 62.2 ± 15.7 µm. Statistical testing revealed that the capsule around the non-coated PCL

TABLE II. The Average Capsule Thickness and Pair-wise Comparisons Between Implant Type. The Result Showed Significant Different with Respect to Capsule Thickness

Type of Plates	Mean of Capsule Thickness (µm) (±SD)	Pair-Wise Comparisons Between Means		
		Non-coated PCL	CHA-coated PCL	Ti
Non-coated PCL	34.3(±15.5)	-	0.0003**	<.0001**
CHA-coated PCL-plate	50.8(±16.4)	0.0003**	-	0.0101**
Ti	62.2(±15.7)	<.0001**	0.0101**	-

** Statistically significant difference ($p \leq 0.05$).

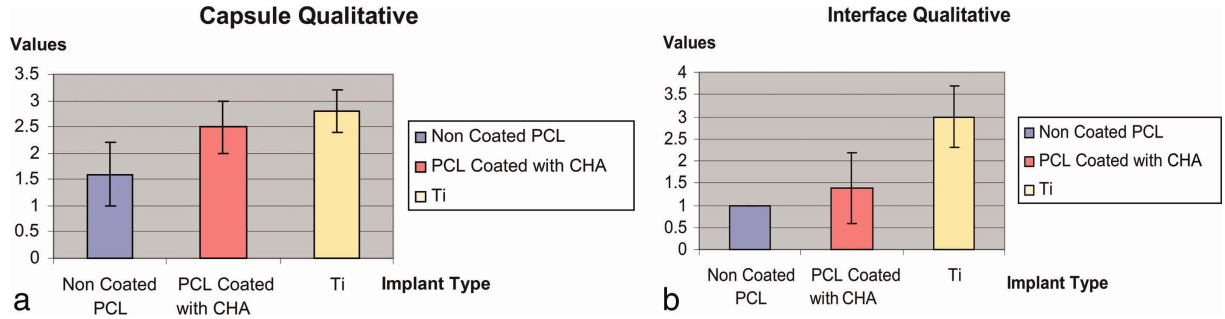

FIGURE 5. Grading scale scores of capsule quality and interface quality for PCL, CHA-coated PCL, and Ti implants. The comparison of percent score distribution of capsule quantity, capsule quality, and interface quality between implant types were analyzed by pair-wise comparison. The significant differences for capsule quality were found between non-coated PCL versus PCL coated with CHA ($p < 0.001$), non-coated PCL versus Ti ($p < .001$), and PCL coated with CHA versus Ti ($p = .042$). Significant differences for capsule interface quality were found between non-coated PCL versus PCL coated with CHA ($p = 0.010$), non-coated PCL versus Ti ($p < 0.001$) and PCL coated with CHA versus Ti ($p < 0.001$). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

plate was significantly thinner compared with the CHA-coated PCL and Ti-plates (Table II). Also, the capsule around the CHA-coated PCL plates was found to be significantly thinner compared to that around the Ti-plates (Table II).

The soft tissue grading scores for capsule quality and interfacial tissue response are depicted in Figure 5. The mean soft tissue grading score for capsule quality of PCL, CHA-coated PCL, and Ti-implants are 1.6 ± 0.6, 2.5 ± 0.5, and 2.8 ± 0.4, respectively. The mean soft tissue grading score for interface quality of PCL, CHA-coated PCL, and Ti-implants are 1.0 ± 0.0, 1.4 ± 0.8, and 3 ± 0.7 (Fig. 5), respectively.

Statistical analysis by Fisher's exact test on global null hypothesis testing showed homogeneity of data distribution for all three implant groups. The comparison of percent score distribution of capsule quality and interface quality between implant types was analyzed by pair-wise comparisons. The results show that all three groups differed significantly relative to capsule quality and capsule interface quality.

DISCUSSION

Soft tissue adherence between host tissues and an implant is important to minimize implant-soft tissue dehiscence, to improve the long-term performance of a device *in vivo,* and to reduce the occurrence of infection. Metallic and polymeric implants are known to become surrounded by a fibrous tissue capsule after their installation in soft body tissue.[3,24,25] Physical properties, such as implant shape, mechanical properties of the implant material, and degree of surface roughness, as well as chemical properties, determine the final soft tissue response.[3]

In this study, rectangular plates composed of different materials, that is, commercially pure titanium (Ti), non-coated PCL, and CHA-coated PCL were inserted subcutaneously into the back of rabbits for 5 weeks. It was hypothesized that (1) the PCL implant would show an improved soft tissue response compared to the Ti-implant, and (2) the CHA coating, as provided to the PCL plates, would further favor the soft tissue reaction. However, histological analysis after retrieval of the implants did not confirm the hypothesis. Overall, the soft tissue response to all implants was very similar, and no direct attachment of connective tissue to the various surfaces was observed.

Clinical observation of the implants after 5 weeks of installation in the rabbits showed that the machined surfaces Ti-plates had migrated over a distance of 0–4 cm. This was more than the coated and non-coated PCL plates, which were found to have migrated 0–1 cm. Such migrational behavior is commonly found when implants are inserted in soft tissue without any additional fixation to the soft tissue layer and is related to the soft tissue adhesion of each particular implant surface. The degree of migration indicates a lack of soft tissue adhesion of the implant surface. The current findings corroborate with an earlier study dealing with the migration of microchips in Beagle dogs.[26] In this study, microchips made of three different materials, that is, bioglass, acid-etched bioglass, and bioglass provided with a polypropylene cap, were installed in the soft tissue around head and shoulder of the Beagle dogs for 16 weeks. Different degrees of microchip migration were observed, which was depending on the location and the used material. The microchips in the shoulder, which had more muscle activity, showed a migration up to the maximum of 11 cm. In contrast, the microchips in the head area moved only to a maximum distance of 2 cm from their insertion point. Furthermore, the microchips made of etched bioglass or provided with a polypropylene cap were found to migrate significantly less than microchips made of just bioglass.[26]

To define the level of soft tissue attachment with the implant surface, we made use of a tissue peel test. Bobyn et al.[27] found that the increased strength of tissue attachment is correlated with implantation time. Similarly, in an earlier pilot study, we demonstrated that specimens at 2 weeks of plate implantation (result not shown) demonstrated a poor soft tissue attachment irrespective of the implant surface finish. Therefore, in the current study, the implantation time was increased to 5 weeks to allow for the maturation of the tissue attachment. Subsequently, the peel test data demonstrated that there was no significant

difference in peel test readings between the different implant surfaces, and therefore, no relevant mechanical effect of implant surface preparation on soft-tissue bonding was observed. However, we found that during the peel test, tissue adhesion between implant and fresh subcutaneous rabbit specimen was fragile, and the peel test required highly delicate tissue manipulation especially when the samples were small in size. As a consequence, the protocol for the tissue peel test still has room for improvement in future studies. Furthermore, the pores and channels in the PCL structure allowed a better maintenance of moisture than the titanium implant. This can inadvertently affect the peel test result, as faster desiccation of the soft tissue on the titanium implant during testing may lead to increased adhesion. In future experiments, environmental control of moisture and temperature should be regulated to ensure that the soft tissue specimens remain in their optimal condition.

No previous studies are available, in which a peel test was done for PCL. Overall, our peel force results were found to be lower compared with previous studies. [27-29] Hacking et al.[28] studied fibrous tissue ingrowth and attachment to porous tantalum after insertion in the dorsal subcutaneous tissue in dogs. A peel test was done using a servo-hydraulic tensile test machine at a rate of 5 mm/min. Peel force at 4, 8, and 16 weeks was reported at 61, 71, and 89 g/mm, respectively.[28] Zhao et al.[29] studied titanium fiber mesh with 84.7% porosity and compared this material with conical implants coated with various compositions of bioactive glass. Ti-mesh was inserted into the dorsal subcutaneous soft tissue and muscles in the back of rats for 8 weeks. Titanium fiber mesh implants showed a relatively high pull-out force in subcutaneous tissue (12.33 ± 5.29 N, mean $\pm$ SD) and in muscle tissue (2.46 ± 1.33 N).[29] Bobyn et al.[27] installed porous metal plates in the subcutaneous tissue of mongrel dogs. The largest metal pore size with the approximate range of 50–200 microns produced a mean peel strength of attachment of 27.5 g/mm after 16 weeks of implantation period. All these high values can be explained by the nature of the implant material used. A highly porous material will allow a better penetration of the soft tissues compared with the current materials.

The histological analysis showed a lack of direct contact between the soft tissue and implant surface. The observed formation of a fibrous capsule around the machined surface titanium implant with the presence of none or very minimal inflammatory cells is similar to a previous study.[3] Titanium is an "inert" material and causes a minimal immune response and foreign body reaction in soft tissue.[30] This is the reason that many commercially available implantable devices (such as pacemakers) are made of medical grade titanium (alloy).

In the present study, coated and non-coated PCL plates were found to be superior compared to the Ti-implant in terms of fibrous capsule thickness. However, the fibrous capsule was found to be less mature and contained more macrophages and inflammatory cells at the tissue–implant interface than the Ti-implants. The surface modification with a CHA coating on the PCL plate increased the surface roughness as shown in the SEM images (Fig. 3). PCL implant with CHA surface coating showed a significant improvement in capsule quality and tissue–implant interface quality, as observed by the reduction of inflammatory cells. This effect can be due to the increased surface roughness as created by the CHA coating. On the other hand, coating of PCL with CHA can also change the mechanical properties of PCL, that is, the material becomes less flexible, which can also affect the soft tissue response.

PCL matrices are known to degrade at low rates by hydrolysis of the ester bonds and break down to their constituent monomer-hydroxycaproic acid, which then undergoes phagocytosis. PCL is characterized by a very low hydrolysis rate, which can vary from months to years.[31] Therefore, the degradation process of PCL during the 5 weeks implantation period in this study was supposed to have no effect on the study result. For PCL coated with CHA, the CHA was still found to be intact at the end of 5 weeks and was clearly visible in the histological sections. Nevertheless, future research has to elucidate the effect of CHA on the biodegradation rate and bone regeneration properties of PCL.

CONCLUSIONS

The data of the current study indicate that none of the materials as well as surface modifications resulted in a superior soft tissue response. The peel test showed that adhesion of the soft tissues did not occur. Although both types of PCL implants showed less migrational behavior compared with the Ti-implants, soft tissue adhesion was not observed for any of the investigated implants, as demonstrated by the peel test data. Fibrous capsule formation around the non-coated and CHA-coated PCL implants was less than that around the Ti-implants. On the other hand, an increased amount of interfacial inflammatory cells was present for all PCL implants compared with the Ti-implants.

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