Effect of Biomimetic Coatings on Periprosthetic Tissue Composition for Osseointegrated Devices

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Disclosures:

Introduction:

Introduction: A viable, long-term percutaneous implant with a permanent skin-seal would represent a major medical breakthrough, reducing infections and healthcare costs for several pertinent percutaneous device applications, especially the percutaneous osseointegrated prosthesis (POP), intended for patients with limb loss[1,2]. The major challenge affecting osseointegrated devices in amputees for direct skeletal bonding has been infection and chronic healing responses at the skin-implant interface. In the case of POP devices, attainment of a stable infection-free, non-migratory skin interface would be a major advancement in the rehabilitation of amputees with short or multiple limb loss, who could not otherwise be fitted with a traditional socket docking system [3-5]. Normal wound healing has been shown to be a complex process that is coordinated in an orderly and efficient manner [6,7]. The effective completion of each healing phase would be even more complex in the presence of a skin protruding percutaneous post for exoprosthesis attachment. Although Type I collagen has been found in normal cutaneous connective tissue, in a healing dermal wound bed, Type III collagen has been shown to be the most abundant type[8,9]. The periprosthetic granulation tissue composition could be used to predict the healing outcomes of percutaneous implants. A biomimetic coating might encourage a permanent healed wound response at the implant interface. It was therefore hypothesized that implants treated with biomimetic coatings, HA and keratin, would show improved healing outcomes at the interface, and produce a periprosthetic tissue that resembles a healed tissue matrix with a high composition of collagen I.

Methods:

Methods: Thirty percutaneous implants, each with an attached porous coated sub-dermal disk, were surgically placed into the dorsal skin of 5 pigs. Each pig had six implants, with one coated with keratin, and another with hydroxyapatite. After 12 weeks, collected periprosthetic tissue samples were snap-frozen with liquid nitrogen. For immunohistochemical staining, the tissue samples were incubated separately with Type I and III collagen antibodies. Each sample was then observed using a confocal microscope. The mean fluorescent signal intensity values within a predefined area of the tissue sections were calculated for each treatment were compared and statistically analyzed. Additionally, the collagen types within the periprosthetic tissue were quantified with ELISA tests. Samples from three areas were tested: baseline tissue, post-euthanasia granulation tissue, and post-euthanasia dermal tissue. A known amount of the granulation and healthy tissues were separately weighed and digested with pepsin in order to get the tissue homogenates. Collagen contents were analyzed and the ratio of collagen I:III from each mixture was calculated.

Results:

Results: The IHC stained photomicrographs showed that the periprosthetic tissue was indeed hypercellular compared to surrounding healthy tissue. The IHC stains that were
specific for collagen I and III indicated that the fluorescent signals densities at the interface were different amongst the samples. Often, the collagen III labels were higher, and the collagen I labels were lower in the post-euthanasia granulation tissue area. However, the HA coated signals did not show a significant difference from the normal tissue. Semi-quantitative immunofluorescent signal densities, as percentage area fractions, were calculated at pre-defined areas. Data indicated that there was more collagen I present in periprosthetic tissue when compared to native dermis. In addition to the semi-quantitative of IHC signal, ELISA analysis data validated the IHC findings. It was found that the collagen I:III ratio within the peri-implant tissue of HA coated implants (5.1:1) was very similar to that of native dermal tissue, which was reported to be in the range of 4-5.5:1 for human skin[10]. Whereas, granulation tissue excised from the keratin coated and control implants showed collagen I:III ratio of 1.4:1 and 0.6:1, respectively.

Discussion: While HA coated implants produced a more limited periprosthetic granulation matrix, keratin coated implants did not. However, the ratio of collagen I to III found within the periprosthetic granulation tissue of keratin coated implants was closer to the healthy dermis than that of the untreated control. The data and the observations further validated our previous finding, which indicated a persistent presence of granulation tissue and continuing wound healing response at the skin-implant interface [11]. There might be multiple mechanisms that arrest the wound healing response and the prevention of a non-migratory skin-seal. This may either be due to impaired or on-going wound healing signals, possibly caused by both biological and mechanical cues at the implant interface. The presence of a high degree of collagen III in the periprosthetic tissue of control and keratin coated implants indicated that the tissue was an ongoing granulation bed. Our data indicated that the granulation tissue seemed to be remodeling towards healed status when HA coatings were used, but remained incomplete as well.

Significance: Ultimately, the significance of this trial was to apply the findings to percutaneous devices, particularly osseointegrated exoprosthetic devices. Previously, the tissues response to various implant materials has been described as a fibrous capsule with varying thicknesses and degrees of inflammation and its composition of collagen types [8]. If the granulation tissue could also be directly linked to the implant materials’ ability to promote complete wound healing at the three-phase junction (where implant, skin, and external environment meet), then the degree of healing responses could also be easily quantified and compared. Through this study, we identified the ratio of collagen I to III as an index for such comparisons. The percutaneous osseointegrated device has the potential to greatly benefit amputees, and discovering the healing mechanisms at the skin-implant interface could move the technology forward.

Acknowledgments:

References:

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**ORS 2014 Annual Meeting**

Poster No: 0673