



# OPEN Surgical considerations towards inducing proprioceptive feedback in dental implants

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Periodontal ligament (PDL) consists mainly of collagen fiber bundles with specialized mechanoreceptors and free nerve endings that connect the cementum of the tooth root to alveolar bone and are vital for dental proprioceptive function. When a tooth is lost and replaced with a dental implant, osseointegration occurs without the intervening PDL, leading to a loss of proprioceptive function. Herein we report the placement, and healthy integration of an advanced dental implant in the socket of rat study models without facilitating the process of osseointegration, that could possibly impart proprioceptive features comparable to those noted in natural teeth. The experimental surgical procedure during dental implant installation in rat models involved various oral tissue structures surrounding the teeth as analogous to those in human subjects and therefore bears a significant clinical relevance. Additionally, the surgical procedure detailed here confers the advantages of its use to investigate not only dental implants but also could be explorative for a wide range of extra-oral implants for improved neural integration.

**Keywords** Rat study models, Experimental surgery, Titanium dental implant, Press-fit dental implants

Partial or complete edentulism is the state of being edentulous i.e. without one or all natural teeth, respectively. Tooth loss, predominantly, occurs due to consequences of dental diseases, such as dental caries or periodontitis<sup>1</sup> which may lead to imbalance in the stomatognathic system<sup>2</sup> and initiating a multitude of extreme ramifications<sup>2</sup>. It is noteworthy that ageing alone has a minor impact on the ability of patients to reduce food into smaller particles, if the confounding factor of tooth loss is controlled for<sup>3</sup>. Furthermore, food stiffness/rigidity is also perceived through the periodontal proprioceptive feature of a healthy tooth relaying sensory information to mesencephalic trigeminal nucleus<sup>4–6</sup> in the midbrain (Fig. 1) during mastication and affects the masticatory force, activity of oral musculature, and mandibular movements all contributing to rhythmic jaw movements, and mashing of food between the teeth<sup>3,7</sup>. Later, the muscle of mastication are inhibited by sensory receptors in the oropharynx through food bolus and initiates the complicated process of swallowing<sup>8–10</sup> where pharynx is transformed into a tract for food propulsion, momentarily<sup>11</sup>. Thus, periodontal proprioception along with the neuro-muscular control of chewing contributes to comminution of the food<sup>3,7</sup> and its propulsion<sup>12</sup> towards alimentary canal<sup>13</sup>. In cases of edentulism, prosthodontic management through dental implants, secured through osseointegration are recommended due to numerous advantages<sup>14</sup> with an estimated projection of its use in roughly 23% of US population by 2026<sup>15</sup> and an increasing trend in dental implants market share of approx. USD 13.01 billion globally<sup>16</sup>.

However, dental implant replacing a lost tooth bears a substantial physiological consequence due to absence of intra-dental and periodontal mechanoreceptors that alters the precise coordination of maxillo-mandibular relation and impacts the discriminatory, directional and masticatory sensation<sup>17</sup>. Although, patients rehabilitated with dental implants have shown enhanced tactile discriminative capabilities & motor function compared to complete denture patients<sup>18</sup>, they do not adequately restore all the oral function to the former stomatognathic privileges<sup>19</sup>. Scientific evidences concludes that the dental implant osseointegration resulting from secondary stability, lacks the specialized periodontium at the interface and its associated functionality such as a *very subtle tactile sensitivity*<sup>20</sup> i.e. periodontal proprioception, leading to altering the precise coordination of oral, pharyngeal, and laryngeal structures<sup>17</sup>; further deviating from the ideal norm of subsequential digestion-

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assimilation process indicating towards an largely uncharted “*missing of periodontal sensory perception*” induced impact on overall health and well-being in humans<sup>13,21–23</sup>.

Hence, to address the limitations of current dental implants<sup>19,24–30</sup> we designed an advanced prototype for dental implants ((Supplementary Methods, Supplementary Fig. 1–8, Supplementary Table 1) specific for inducing proprioceptive features (Fig. 1) and were successful in accurately installing (Fig. 2) and integrating them (Fig. 3) in the tooth socket of rat study models. While confirmatory proprioceptive status will be examined in animals with the specific procedures in the future, we anticipate that the simple surgery and bioengineering strategy implemented in our initial trial evaluations could drive progress in creating new design concepts for the modified dental implant integration that doesn't involve the conventional osseointegration process. Additionally, the procedural details here will also provide insight into modifying a wide range of other neuro-prosthetics and nerve rehabilitation devices in the direction of superior neurophysiological integration.

## Methods

### Dental implant prototype

The test implants were fabricated with a shorter dimension in comparison to the length of original tooth for sufficient interocclusal space and were later coated with nanofibers (Supplementary Methods). The Growth factor was adsorbed during the coating onto the surface intermittently, proving a multi-layer of orderly pile stack of growth factor adsorbed layers (Supplementary Methods). The undifferentiated immortalized stem cells (Supplementary Methods) were seeded on the surface of the coating with increased concentration of cells in the middle 3rd, lingually.

### Animals

Male Brown Norway rats ( $n = 3 + 3$ ) aged 12 weeks, weighing ~225–245 gms upon initiation of the study were purchased from Charles River Breeding labs. Rats were housed with food and water provided *ad libitum*, light in 14:10 h light: dark cycles, and housed at ambient 22 °C ( $\pm 1$  °C) temperature with 30–70% humidity.

After a 3-day acclimatization period, the rats were assessed and found to be free of clinical signs of diseases, with normal posture, movement, respiration cycle, cardiovascular status etc. For comparative evaluation hematological, cytokines parameters, temperature, weight and H&E-stained sections of left submandibular cervical lymph node of representative rat models (with and without implants) were obtained at the end of the trial period (Supplementary Fig. 9.) (Supplementary Tables 2–5.). At the end of the trial period the rats were euthanized using carbon dioxide (CO<sub>2</sub>) inhalation to induce asphyxiation, followed by cervical dislocation as a secondary euthanasia.

### Implant surgery

Animals ( $n = 3$ ) were briefly anaesthetized with 70 mg kg<sup>-1</sup> ketamine and 10 mg kg<sup>-1</sup> Xylazine. Povidone-iodine swab sticks (Medline, MDS 093902) and 2% chlorhexidine were used to disinfect the intraoral region. Pre-surgical evaluations were meticulously performed for the left mandibular tooth, its surgical anatomy, the length of the crown and its occlusion, interocclusal relationship, alveolar ridge, potential mandibular implant site, etc. Besides the usual oral surgical instruments, modified surgical blades from the hypodermic needles (Exel Int. 25 G, Ref.26403) were fabricated, by flattening, and sharpening their edges. During the surgery, the sterile modified blades were placed into the gingival sulcus of the mandibular left incisor, distally, with gradual tearing of the distal gingival fibers and advancing apically, extending far down, progressing and severing the deeper attachment fibers. Thereafter, the blade was gently proceeded further, in the periodontal space, moving circumferentially, surrounding the tooth, gradually towards mesio-apical orientation, carefully maneuvering around the external contour of the tooth and completely detaching the mesial attachment fibers loosening the tooth (Fig. 2). The tooth was later grasped with tweezers (Harfington, Uxcell, Ref:1174861) gently luxated and extracted. The dental implant coated with immortalized undifferentiated rat dental pulp stem cells (Supplementary Methods) was press fitted and fixed in its natural position in the fresh socket. A cyanoacrylate adhesive dressing (PeriAcryl® 90, GluStitch Inc., Delta, Canada) was used to seal and secure the interface of titanium implants and peri-implant soft tissue from rest of the oral cavity (Fig. 2). Meticulous preoperative and postoperative radiological evaluation (Skyscan 1176 High Resolution Micro-CT Scanner, Bruker) relevant to maxilla-mandibular structures, precise placement of the dental implant and their relation to adjacent structures (Fig. 3) etc. were carried out. For management of postoperative pain, analgesics such as buprenorphine hydrochloride 0.05 mg kg<sup>-1</sup> was used.

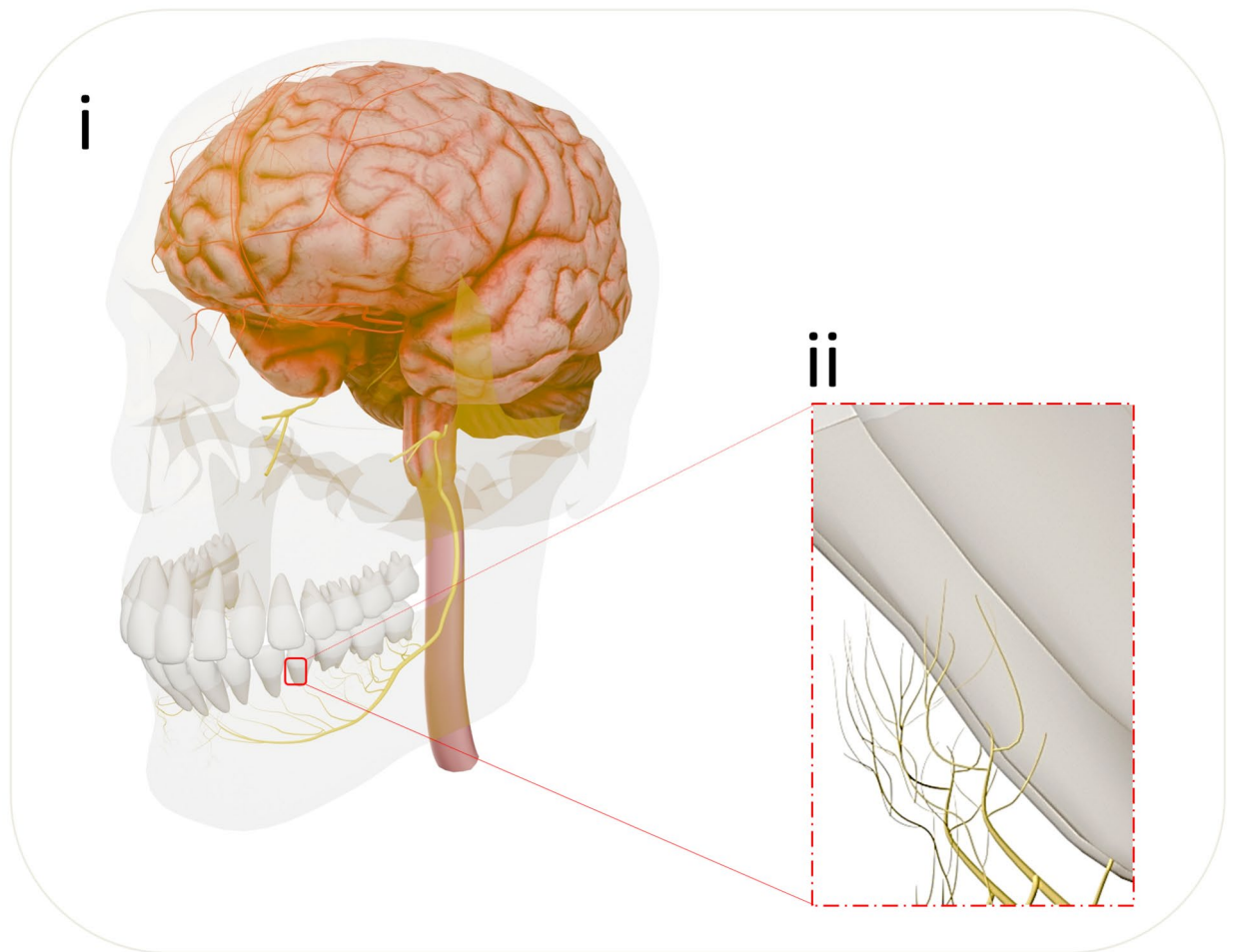
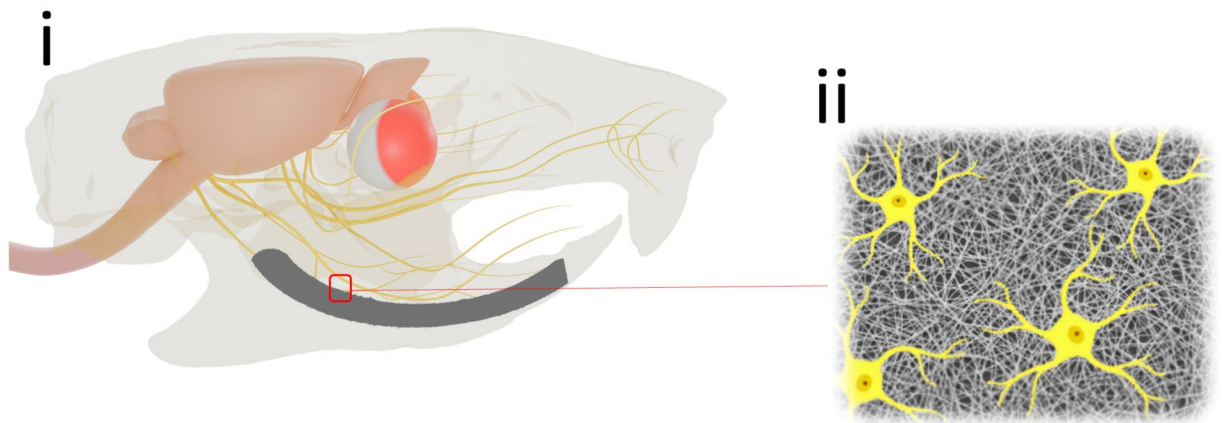
### Post-operative care and housing

Animals were housed individually and during post-anesthesia warming phase, a heating pad, set at ~37 °C, was placed beneath each recovery cage. During the post-surgery recovery period, all the animals have 14 h:10 h light/dark cycle and had access to gel diet (DietGel® Recovery & DietGel 76 A, Clear H<sub>2</sub>O) along with standard food and water *ad libitum*.

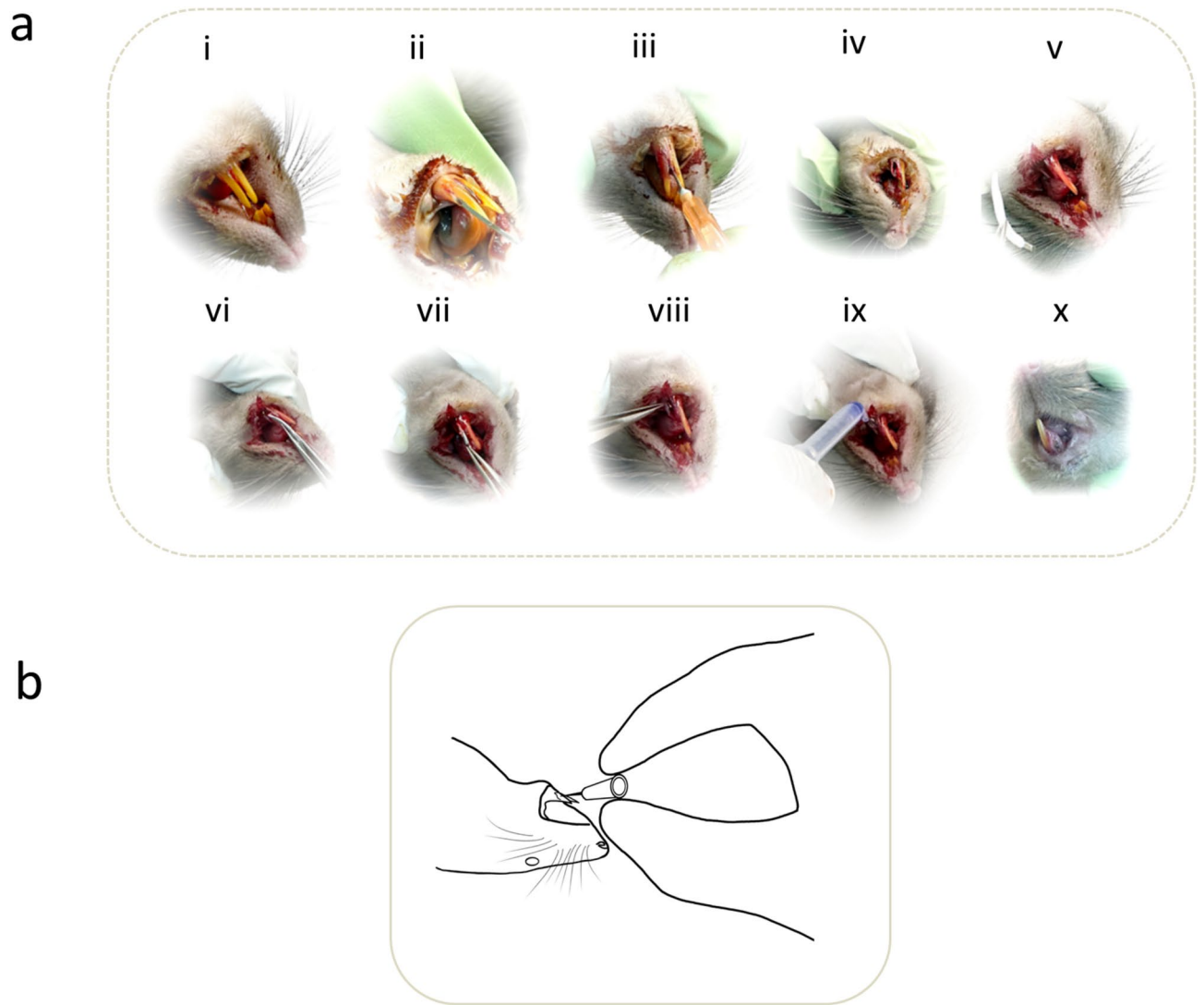
We confirm that the animal experiments were executed in conformity with the relevant guidelines and regulations established by the National Institutes of Health and institutional guidelines with the approval of Tufts University's IACUC (Protocol #B2020-156).

## Results

All the animals survived the whole experimental time, and no operative or postoperative complications were encountered. The clinical and macroscopic evaluation revealed that all the prototypes for dental implants were well fixed in their respective dental sockets at the end of the trial period (Supplementary Video). All the rats presented healed peri-implant mucosa with no evidence of exudation, inflammation or crusting. Micro-CT

**a****b**

**Fig. 1.** Translational implication of the trial investigation: **(a) i**, The human brain with the maxillary and mandibular teeth are connected through the trigeminal nerve. For reasons of simplification, only the inferior alveolar nerve arising from the mandibular branch of the trigeminal nerve (CN V3) providing sensory innervation to the mandibular teeth, gingiva, and dental sockets is shown. **(a) ii**, Besides dental pulp innervation, the roots of the mandibular teeth are covered by the free nerve terminals mostly from the inferior or mental division of the mandibular branch of the trigeminal nerve. **(b) i**, Through an experimental surgical protocol, the left mandibular central incisor in the rat study models were extracted and subsequently the elastomeric nanofibre coated dental implant with stem cells were placed in the dental socket. Accordingly, appropriate cues were engineered for guiding the stem cell's fate and differentiation towards neural cells on the biodegradable coating **(b)iii** influencing a modified integration where the differentiated neural cells present in the regenerated neo-tissue complex may anastomose with the severed/terminal sensory branches in the interior wall of the dental socket arising from the trigeminal nerve.



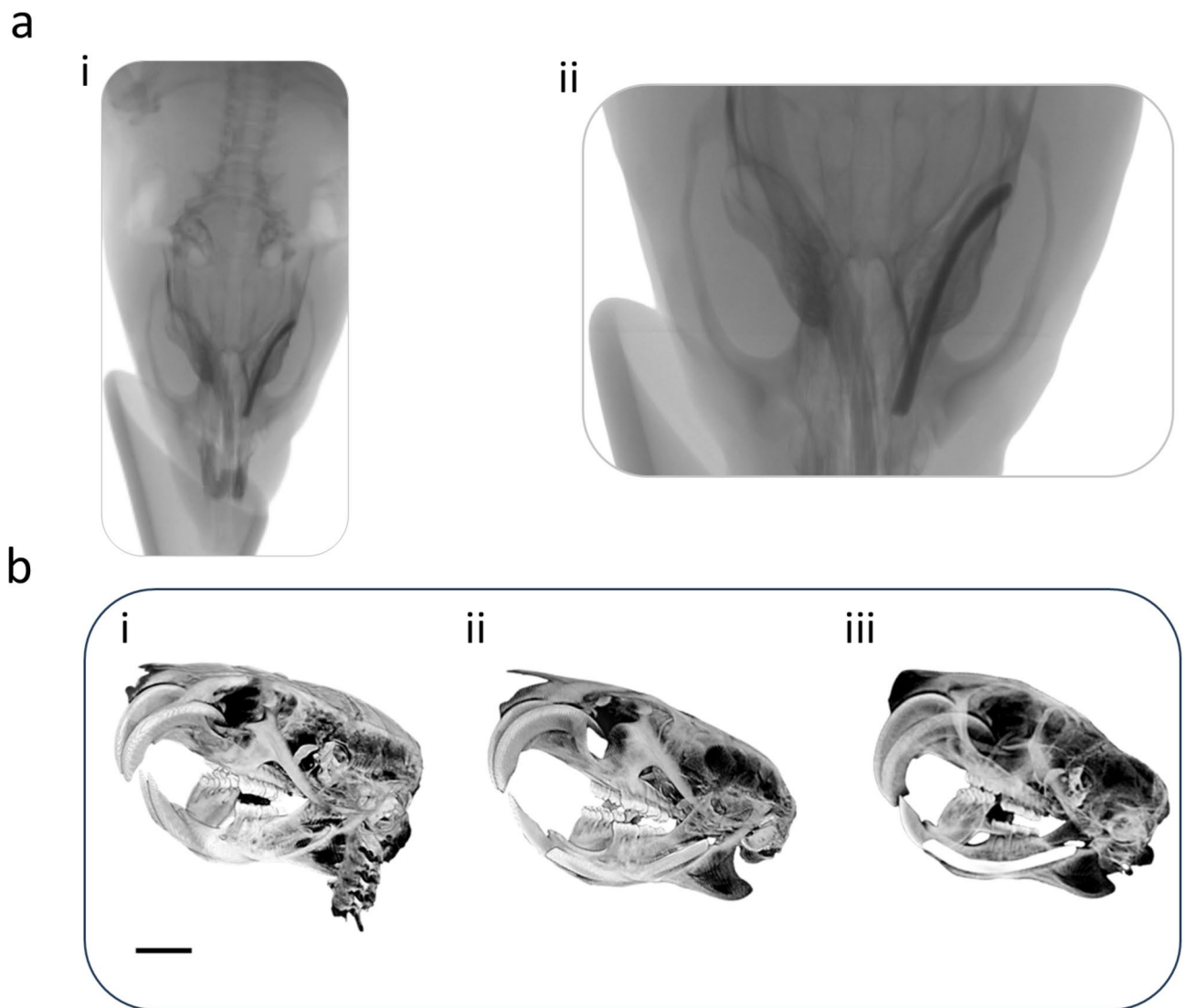
**Fig. 2.** The details of the intraoperative photographs of the representative rat model manifesting the experimental surgical technique for installing titanium dental implant in the mandible. (a) i, Unoperated normal and healthy mandibular central incisors. (a) ii, Careful and gentle insertion of the customized blade into the gingival sulcus distally, gradually advancing towards the center of the tooth and progressively severing the attachment fibres towards the apical orientation. (a)iii, Gentle insertion of the customized blade into the mesial gingival sulcus, and later advancing into the periodontal space with the tip of the blade angled towards the long axis of the incisor and severing the respective attachment fibres around the entire tooth circumference. (a) iv, The structural integrity of the tooth socket is well maintained after gently extracting the loose tooth. (a) v-viii, Elastomeric nanofibrous coated dental implant with stem cells is press-fitted in the dental socket. (a) ix, A tissue adhesive was used to cover the peri-implant region. (A)x, Peri-implant tissue healing after 48 h. (b) Gentle holding of the surgical blade during the experimental surgery ensuring the least traumatic way to divide the tissues.

investigation after 6 weeks post-implantation revealed distinct peri-implant radiolucency as a narrow radiolucent space in the range of 0.7–0.9 mm between the alveolar bone and the dental implant indicating absence of osseous/calcified characteristics in the integrating tissue (Fig. 3). Notably, absence of cervical lymphadenopathy throughout the investigation, along with the comparative histological evaluation (Supplementary Fig. 9). of the left submandibular lymph node, blood biochemistry, hemogram, cytokine levels, temperature, weight (Supplementary Tables 2–5) etc. indicated uneventful recovery.

### Discussion

As periodontium in the healthy natural tooth are equipped with highly specialized periodontal mechanoreceptors<sup>31,32</sup>, it is unlikely that any regenerative intervention directed towards proprioceptive titanium dental implant will produce a physiologic outcome that is equivalent to that of a healthy and true periodontium. Conversely, some reports also highlight about the presence of periodontal mechanoreceptors even after the





**Fig. 3.** Radiological evaluation. (a)i-ii, Plain radiographs of dental implant after six weeks of dental implant surgery. (b) i Micro-CT images of rats with no dental implants, (b)ii, immediately after placing the implant, and (b) iii, after six weeks post-surgery. Distinct peri-implant radiolucency with no appreciable bone-to-implant contact is noted for both plain radiographs and micro-CT images. Image scale bar in (b) represents 10 mm.

tooth extraction<sup>33</sup> and that had led to investigation of reinnervation in relation to titanium dental implants<sup>34</sup> but with no success.

It is largely agreed that the sensory component of the periodontal ligament contains rich sensory non-encapsulated terminal receptors including free nerve endings and specialized Ruffini-like endings<sup>35</sup>. In humans, the periodontium receives innervating nerve fibers<sup>36,37</sup> mostly through the apical region and some course through the lateral foramina in the alveolar bone<sup>38</sup>. Following routine exodontic procedures, the nerve fibers innervating the periodontal ligaments and the pulp are crushed and severed. During the subsequent period of normal socket healing<sup>39</sup> there is a possibility that these traumatized and residual nerve fibers may regenerate into and through the soft tissue of the socket, innervating the periosteum or alveolar mucosa. Alternatively, they may form a traumatic or amputation neuroma within the jawbone<sup>40</sup>.

Hence, our proof-of-concept trial deals with targeted repairing of these injured terminal nerve endings instead of the whole periodontium, that are present as an extension of the trigeminal system at the interface of the immediately placed dental implant and alveolar bone through a significantly less traumatic experimental surgical protocol, thereby restoring the neural circuitry in an otherwise intact dental proprioceptive route that communicates from the interface of a tooth root/dental implant to the mesencephalic nucleus in the midbrain.

Consequently, for achieving our objective a modified integration of dental implants is crucial and accordingly the advanced prototype for dental implants were installed based on the press-fit phenomenon<sup>41</sup>. Additionally, multiple innovative strategies were implemented to engineer the dental implant integration that is different from the usual or conventional “osseointegrative” way; such as coating dental implants with elastomeric biodegradable

nanofibers, multilayer incorporation of hyperstable FGF- $\beta$  in the coating, seeding exogenous rat's dental pulp stem cells in the coating that were concentrated in the region corresponding to the alveolar half of the lingual periodontal ligament and were based on the neuroanatomical details of the rat's incisor<sup>42–46</sup> etc.

Finally, and above all, the requisite atraumatic tooth extraction were performed on rat study models by using customized flexible & sharp blades. These blades were fabricated by flattening and sharpening the edges of the syringe needles for gently disengaging the periodontium and extracting the complete tooth with least trauma to the peri-dental tissue for maintaining the structural integrity of the socket and preserving the maximal severed periodontium is the interior wall of the socket containing the unencapsulated nervous elements such as Ruffini-like corpuscles and free nerve endings.

Upon completing the immediate dental implant placement in the socket, the deformed and compressed elastomeric nanofibrous coating, slowly resumes its shape conforming the interior dimension of the socket ensuring a snug or tight fit and further resulting the attached exogenous dental pulp stem cells on the coating to directly interface the aforementioned nervous elements. This closely fit status of the dental implant with no appreciable signs of mobility may be comparable to *primary stability* of the conventional titanium dental implants, that are observed and favoured during surgical placement and arises from the mechanical friction between implant surface and the surrounding bone<sup>14,47</sup>.

Likewise, herein, over a period of time & under the influence of hyper stable fibroblast growth factor 2 (FGF 2)<sup>48</sup> in the coating, orthotopic environment<sup>49,50</sup> and experimental surgery, the elastomeric nanofibrous coating with stem cells in the dental socket slowly deteriorates with progressive repairing of the terminal nerve endings<sup>48</sup> including possible neural anastomosis and gradually replacing the interfacial space occupied by the elastomeric coating with neo-tissues bridging alveolar bone and implant surface having features dissimilar to osseous tissue yet could be analogous to well-established *secondary stability*<sup>14,47</sup>, in the healing stages that completes the osseointegration process, noted in the conventional dental implants. Convincingly, the 6 weeks old integrated prototypes were neither tender to percussion or pressure nor was mobile (Supplementary video)<sup>51</sup>, together with the distinct per-implant radiolucency (Fig. 3), the occurrence of the purely fibrous integration<sup>52</sup> or fibro-osseous integration<sup>53</sup> were therefore excluded.

Although this innovate surgical trial was performed on small sample size of preclinical study models, the surgical anatomy of peri-dental region specifically the minimally invasive experimental surgical technique limited only to connective tissue attachment fibers such as periodontium, marginal gingiva, attached gingiva, etc. and the modifications in the prototype of titanium dental implants, bears a close resemblance to actual cases managed in clinical scenario and indicates that the modified integration of the prototype dental implants towards proprioceptive function could be a formidable alternative to its well established osseointegrative counterpart. However, such engineered integration results in dental implant to be *proprioceptive* needs to be confirmed especially through advanced neurodiagnostic imaging techniques for prompting a clinical trial.

Advantageously, reports in the literature also explains about the rodents such as mole rats where extraordinary brain organization i.e. nearly one-third (31%) of primary somatosensory cortex is devoted to the representations of the upper and lower incisors<sup>54</sup>. Therefore, assuming homology of the neuro-anatomical organization across species with aradicular hypsodonty in terms of both somatosensory representation and the resulting functional connectivity, the similar prototype implants for mandibular incisors with the exact surgical procedures described here will be investigated for proprioceptive function on Brown Norway rats (*Rattus norvegicus*) in the next phase of the trial.

## Limitations

Variations in technique among surgeons performing the same procedure can influence the consistency of outcomes.

## Data availability

All data supporting the findings of this study are included within this published article and its supplementary materials.

Received: 23 October 2024; Accepted: 23 April 2025

Published online: 30 April 2025

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## Acknowledgements

The authors would like to express sincere gratitude to the Bray Lab and Nano Lab, at Tufts University School of Engineering and the George J. Kostas Research Institute for Homeland Security for providing access to advanced facilities that were essential to the completion of this research project.

## Author contributions

Siddhartha Das, Qisheng Tu, Jake Chen, Subhashis Ghosh, Zoe Xiaofang Zhu: Conceptualization, Methodology. Siddhartha Das: Implant fabrication, Coating, Surgery. Siddhartha Das: Writing- Original draft preparation. Siddhartha Das, Subhashis Ghosh: Visualization, Investigation. Jake Chen, Qisheng Tu: Supervision. Siddhartha

Das, Qisheng Tu, Jake Chen: Writing- Reviewing and Editing.

### Funding statement

The authors would like to acknowledge the support from the National Institutes of Health (NIH) with grants DK131444, DE30074, DE25681 and DE32006 to Jake Chen. This study was conducted in accordance with the Declaration of Helsinki and Tufts University policies.

### Declarations

### Competing interests

The authors declare no competing interests.

### Ethical approval

All animal procedures were compliant as per the relevant ethics regulations established by the National Institutes of Health and institutional guidelines with the approval of Tufts University's IACUC (Protocol #B2020-156). All animal procedures were conducted in accordance with the ARRIVE guidelines.

### Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-99923-8>.

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