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PROJECT COMPLETION REPORT

1. **Project Number** : 8092
2. **Title of the Project** : **Biological Evaluation of Laser Rapid manufactured Ti Porous Structures**
3. **Funding Agency Name** : Board of Research in Nuclear Science(BRNS)-Department of Atomic Energy(DAE)
4. **Project Reference Number provided by the Funding Agency:**

   Sanction Number: 37(3)/14/29/2014-BRNS 0706 dated 18/06/14

5. **Principal Investigator (Name & Address) :**

   Dr A .Sabareeswaran,
   Scientist-F & Department Co-ordinator, Histopathology lab, Div of Experimental Pathology, Department of Applied Biology, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and technology, Thiruvananthapuram, Kerala 695012

6. **Co-Investigators (Name & Address):**

   i. **Dr P.V.Mohanan**, Scientist-G, Div of Toxicology, Department of Applied Biology, Biomedical Technology Wing, Sree Chitra Tirunal Institute for Medical Sciences and technology, Thiruvananthapuram, Kerala 695012

   ii. Name of Project Collaborator & Affiliation:
   Dr. C P Paul, Head, Laser Additive Manufacturing Lab &
   Associate Professor, Homi Bhabha National Institute,Raja Ramanna Centre for Advanced Technology, PO:RRCAT, Indore (MP) 452 013

7. **Implementing Institution** : Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram, Kerala 695012

8. **Collaborating Institutions** : Raja Ramanna Centre for Advanced Technology, PO: RRCAT, Indore (MP) 452 013

9. **Date of Commencement** : 17.08.2014

10. **Duration** : 3 years

11. **Date of Completion** : 31.12.2017

12. **Objectives as approved :**
    1. LRM of porous structures of Titanium having various mechanical properties close to natural bone using various LRM strategies
    2. Evaluation of cytocompatibility and biocompatibility of laser rapid manufactured porous titanium structures

13. **Deviation made from original objectives if any, while implementing the project and reasons thereof :**

    NIL

14. **Field/Experimental work giving full details of summary of methods adopted, data collected supported by necessary tables, charts, diagrams and photographs :**

    NA

15. **Detailed anaylsis of results :**

    NA

16. **Summary sheet of not more than 2 pages under following heads :**
    (Title, Introduction, Rationale, Objectives, Methodology, Results, Translational Potential)

    Laser rapid manufactured Titanium (LAM Cp-Ti.) porous structures were manufactured using computer aided designing method which was evaluated for their safety and efficacy in vitro and in vivo in rabbit bone defect model. This implant is supposed to support or enhance bone growth and new bone formation in case of damage to the bone. Titanium is a good candidate material used for bone tissue engineering. In this project, we evaluated a new method of computer assisted laser based manufacturing of Ti implants, to see the effect of this new method of structural designing has any profound effect on the surface properties of LAM Cp-Ti and biological safety evaluation when used as medical implants.

    These implants were first evaluated in cell culture systems (in vitro) to determine the cytotoxicity and cyto compatibility. These studies were done based on ISO 10993 part 5, biological evaluation of medical devices. In vitro studies using L929 cells indicated that the implant is non-cytotoxic and cytocompatible. Further, these Ti implants were evaluated for their potential to induce osteogenesis as they were to be used in bone regeneration studies. These studies indicated that the LAMCp-Ti implant was osteo inductive and has the potential to induce osteogenesis or new bone formation by rat mesenchymal stem cells in comparison with non-induced control. The LRM Ti porous structures were modified using electrochemical anodization to form surface nano tubules as an additional deviation from the project aims. This modification was made aiming at drug incorporation for supporting osteogenic induction and differentiation. The *in vitro* evaluated LRM Ti porous structures were then assessed in vivo in rabbit femoral defect models for biological safety and efficacy determination. Gross observations and the histological analysis revealed bone healing and new bone formation at the interface in both LAMCp-Ti(test) and Cp-Ti(control) groups. New bone formation at the implant-bone interface at one, three and six months post implantation was clearly indicating osteointegration and osteogenesis at implant bone interface. Gene expression study was conducted to analyze the

expression of genes involved in bone formation also indicated that the bone –implant interface had elevated levels of miR-29 a,b,c, (micro RNA) which can regulate RUNX2, collagen type I and SPARC genes there by regulating osteogenesis. To conclude the newly synthesized LAMCp-Ti porous materials were found to be biocompatible with potential to promote new bone formation as evaluated in rabbit bone injury model.

17. Contributions made towards increasing the state of knowledge in the subject :

- Synthesised porous structures of titanium using LRM technique at RRCAT, Indore
- The Laster rapid manufactured Ti (LAM Cp-Ti.) porous structures were found non cyto toxic and cyto compatible based on ISO 10993 part 5, biological evaluation of medical devices.
- The implants were also found to be osteoinductive (supporting and inducing osteogenesis) in experiments with rat mesenchymal stem cells.
- The LRM Ti Porous structures were modified using electrochemical anodization to form surface nano tubules aiming at drug incorporation.
- The LRM Ti porous structures were assessed in vivo as per ISO10993-6 in rabbit femur implant model and was found to support bone healing and new bone formation.

18. Conclusions summarising the achievements and indication of scope for future work :

Synthesised porous structures of titanium using LRM technique at RRCAT, Indore

LRM Ti Porous structures were modified using electrochemical anodization to form surface nano tubules aiming at drug incorporation.

The LRM Ti porous structures were assessed in vivo as per ISO10993-6 in rabbit femur implant model and was found to support bone healing and new bone formation.

To conclude the newly synthesized LAMCp-Ti porous materials were found to be biocompatible with potential to promote new bone formation as evaluated in rabbit bone injury model.

Future custom made Titanium based medical prosthesis using LRM technique shall be explored.

19. Science and Technology benefits accrued :

a. List of research publications with complete details :

b. Manpower trained on the project :

i. Research Scientists or Research Fellows	**:**	**ONE JRF and THREE MPhil**
ii. No. of PhD's produced	**:**	**-**
iii. Other Technical Personnel trained	**:**	**Three**
c. Patents taken, if any	**:**	**-**
d. Products developed, if any	**:**	**-**

20. Abstract: (In 300 words for possible publication in ..... Bulletin)

a. Background:

Laser rapid manufactured Titanium (LAM Cp-Ti.) porous structures were manufactured using computer aided designing method which is supposed to support or enhance bone growth and new bone formation in case of damage to the bone. Titanium is a good candidate material used for

bone tissue engineering. In this project, we evaluated a new method of computer assisted laser based manufacturing of Ti implants, to see the effect of this new method of structural designing has any profound effect on the surface properties of LAM Cp-Ti and biological safety evaluation when used as medical implants.

b. **Materials:**
These studies were done based on ISO 10993 part 5, cytotoxicity evaluation of medical devices. In vivo studies as per ISO 10993-6 local effects after implantation using rabbit bone implantation were carried out. Further, these Ti implants were evaluated for their potential to induce osteogenesis as they were to be used in bone regeneration studies.

c. **Results:**
These implants were first evaluated in cell culture systems (in vitro) and results indicated non cytotoxicity and cyto compatibility. Further, in vitro bone regeneration studies indicated that the LAMCp-Ti implant was osteo inductive and has the potential to induce osteogenesis or new bone formation by rat mesenchymal stem cells in comparison with non-induced control. In vivo bone implantation study revealed bone healing and no adverse tissue response both in control and test implant group indicated that the implant was biocompatible.

d. **Conclusion:**
To conclude the newly synthesized LAMCp-Ti porous materials were found to be biocompatible with potential to promote new bone formation as evaluated in rabbit bone injury model.

21. **Procurement/Usage of Equipment: NIL**

a. **Details of Equipment:**

Sl. No.	Name of Equipment	Make/ Model	Cost (Rs.)	Date of Installation	Utilisation	Remarks regarding maintenance breakdown

b. **Suggestions for disposal of equipment(s):**

NA

1/12/23
A. SABAREESWARAN
Scientist-G
(Name and Signature of PIs with date)

Routing: *Signed copy of "Project completion Report" by PI → root@sctimst.ac.in, rpc@sctimst.ac.in*