Regenerative therapies
Current & Future Scenarios

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Director – Mother cell regenerative centre

Learning Objectives

At the conclusion of this presentation, the participant will be able to:

1. Identify evidenced-based recognized pathways for the treatment of a diabetic foot ulcer/infection.
2. Identify safety & efficacy in bone marrow concentrate and administration recommendations for treatment of the diabetic foot infection.
3. Identify need of growth factors and regenerative factors including additional pharmacological support for the management of a diabetic foot ulcer and other related indications.

DIABETIC FOOT
CRITICAL LIMB ISCHEMIA

Arch Iran Med. 2016 Jun;19(6):388-96. doi: 0161906/AIM.004.

Safety and Efficacy of Repeated Bone Marrow Mononuclear Cell Therapy in Patients with Critical Limb Ischemia in a Pilot Randomized Controlled Trial.

Molavi B[1], Zafarghandi MR[1], Aminizadeh E[2], Hosseini SE[3], Mirzayi H[2], Arab L[2], Baharvand H[3], Aghdami N[3].

- No. of Patients 22
- No of patients with single dose = 11
- No of patients with multiple dose (4) = 11
- Followup period = 2 years
- no reported adverse events
- http://clinicaltrials.gov/ct2 show/NCT01480414
- significant improvement in Ankle-Brachial Index, Visual Analog Scale, pain-free walking distance, and Wagner stage as well as reduction in ulcer size

Long-Term Clinical Outcomes Survey of Bone Marrow-Derived Cell Therapy in Critical Limb Ischemia in Japan

Circ J 2018; **82**: 1168–1178
doi:10.1253/circj.CJ-17-0510

KONDO K et al.

- Retrospective, observational study
- No of patients = 345 (10 hospitals)
- Cell type = autologous bone marrow-derived mononuclear cells
- Followup period = 31.7 months (longest)
- No reported adverse events
- Therapeutic angiogenesis using autologous BM-MNC implantation may be feasible and safe in patients with no-option CLI, particularly those with CLI caused by TAO or CDV

Dental pulp stem cell for Diabetic foot

Journal of the Indian Dental Association
Tamil Nadu State Branch

JIDAT
Journal of the IDA Tamil Nadu

Volume 4 Issue 15
Oct. - Dec. 2012

www.jidat.in

DENTAL PULP STEM CELLS FOR TREATING UNHEALED DIABETIC FOOT ULCER: A PIONEERING ATTEMPT :

Dr. Sankaranarayanan[1] M.D.S., **Dr. P. Ramachandran**[2] M.S., Mch., **Dr. V. R. Ravi**[3] M.B.B.S., M.S., **Dr. Divya A**[4], MDS,

1. Prof& Head Department of Oral Pathology, Srimoogambigai Institute of Dental Sciences, Kulasekaram.
2, 3. Consultant Orthopedic Surgeon, Martuthi Hospital & Director, Mother Cell Regenerative Center
4. Reader, Department of Oral Medicine and Radiology, J.K.K Nattaraja Dental College, Komarapalayam, Namakkal District, Tamilnadu, India.

Dental pulp stem cell for Diabetic foot

PRE OP

POST OP 1MONTH

POST OP 6MONTHS

Image Source: Mothercell Regenerative Centre

www.mcrcindia.com

Diabetic Ulcer With Cord Tissue Stem Cells

Pre Op

Post Op
06.08.12

POST OP
18.12.12

POST OP 6 MONTHS

Critical limb ischemia CASE 1

PRE OPP

POST OPP – 1 YEAR

CLI of renal Failure Patient

Pre Op

Post Op 15 days

Post Op 1 month

Image Source: Mothercell Regenerative Centre

www.mcrcindia.com

AUTOLOGOUS BMMNC

FOR ANGIOGENESIS

TAO

Pre Op

Post Op 6 Months

Image Source: Mothercell Regenerative Centre

www.mcrcindia.com

OSTEOARTHRITIS

Role of Bone Marrow Concentrate

Journal of Indian Orthopaedic Rheumatology Association; January-June 2017:3(1);8-14

Original Research Article DOI: 10.18231/2455-6777 .2017.0002

Intra-articular injection of bone marrow concentrate protocol for Osteoarthritis – A preliminary report with 12 months follow up

VR Ravi[1,*], Avinash Gandhi[2], S. Sankaranarayanan[3], K. Manimaran[4]

Stem cell therapy for Cartilage Regeneration in O.A.Knee @ MCRC – 30 cases

INCLUSION CRITERIA

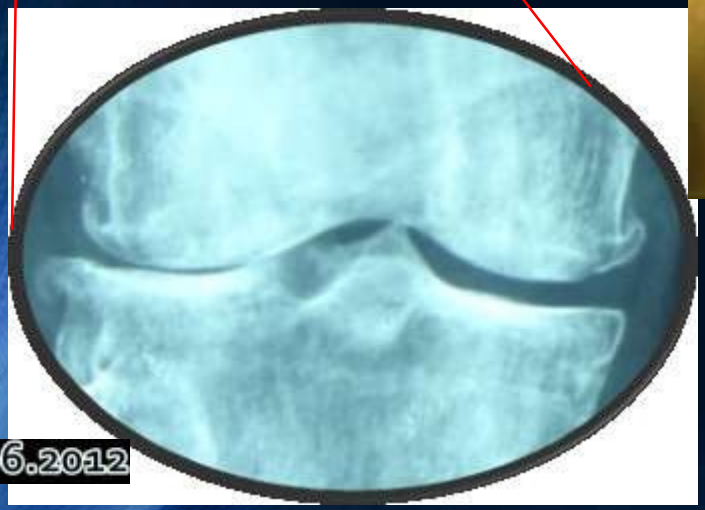
- OA with Renal Failure (Drug induced)
- OA in patient <50 yrs of age
- Previously deformed Anatomy

EXCLUSION CRITERIA

- Gross Deformity of Knee
- Patients on cancer drugs / long term steroids

Longest Follow up – 6 years

Stem cell therapy for O.A.Knee.



DURATION OF PAIN RELIEF

Age Group	Duration of Pain Relief
41-50 Yrs	Max. 3 Years
51-60 Yrs	Max. 2 Years
61-70 Yrs	Max. 2 Years
71-80 Yrs	3 – 6 months

Tissue Engineering & Functional rehabilitation – An Audit

OSTEORADIONECROSIS

- Debilitating complications
- Occur after radiotherapy in patients with head and neck cancer
- Incidence is around 4 and 30 % of patients who undergo head and neck radiotherapy
- Conservative treatment
    - antibiotic use
    - sequestrostomy
    - hyperbaric therapy
- may be enough for patients with limited ORN

Aristeidis et al. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. International Dental Journal 2018; 68: 22–30

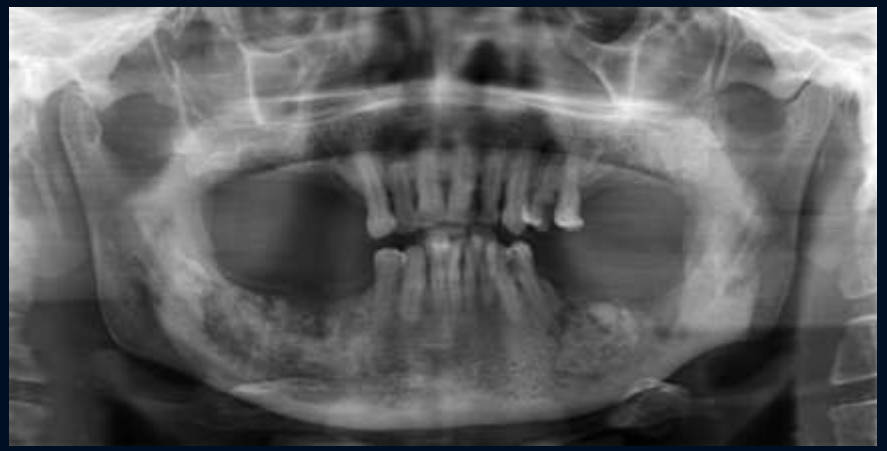
Comparision of cell based rx with hyperbaric oxygen RX

Image Source: Mothercell Regenerative Centre

Post OP Comparison

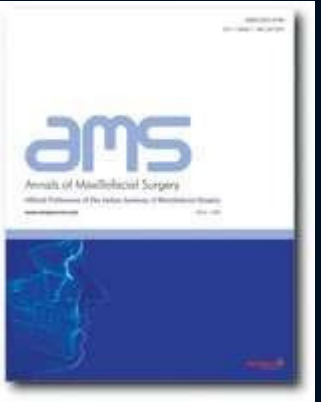
PRE OP

4 MONTHS POST OP



Treatment of Osteoradionecrosis of Mandible with Bone Marrow Concentrate and with Dental Pulp Stem cells.

Original Article - Prospective study



Manimaran K, Elangovan S, Chandramohan M, Mahendraperumal S, Sankaranarayanan S, Ravi V R.

Annals of Maxillofacial Surgery | July - December 2014 | Volume 4 | Issue 2

Front Physiol. 2015; 6: 213.
PMCID: PMC4526817
Published online 2015 Aug 6. doi: 10.3389/fphys.2015.00213

Manufacturing of dental pulp cell-based products from human third molars: current strategies and future investigations

Maxime Ducret,[1,2,3] Hugo Fabre,[1] Olivier Degoul,[4] Gianluigi Atzeni,[4] Colin McGuckin,[4] Nico Forraz,[4] Brigitte Alliot-Licht,[5] Frédéric Mallein-Gerin,[1] Emeline Perrier-Groult,[1] and Jean-Christophe Farges[1,2,3,*]

[1]Laboratoire de Biologie Tissulaire et Ingénierie thérapeutique, UMR5305 Centre National de la Recherche Scientifique/Université Claude Bernard Lyon 1, Lyon, France

DP-CBMP Uses

Over recent years, DP-CBMP were clinically tested with the aim to regenerate human craniofacial bone. DP-CBMP were implanted, in association with a collagen I-based sponge scaffold, in mandibular bone sockets in a phase I clinical trial (d'Aquino et al., 2009). Three years after DP-CBMP grafting, the tissue regenerated in the graft site was compact bone (Giuliani et al., 2013). Case reports of osteoradionecrosis treatment using DP-CBMP were also reported (Manimaran et al., 2014). The angiogenic, neurogenic and odontogenic potential of DP-CBMP was also successfully tested in preclinical studies (Gandia et al., 2008; Iohara et al., 2009; Sakai et al., 2012; Ishizaka et al., 2013). In addition, a phase I clinical trial is currently under progress to evaluate the DP-CBMP potential to regenerate the human dental pulp (Nakashima and Iohara, 2014). Despite these successes,

We recently proposed the use of impacted third molars between Nolla's developmental stages 5 (crown almost completed) and 7 (one third root completed). The presence of large, open apices in teeth without roots or with roots partially developed allows for an easy access to the pulp tissue and its gentle, atraumatic extirpation from the enamel/dentin shell with fine tweezers. It avoids the cell stress resulting from the crown-root mechanical separation with a drill or a clamp that is necessary for recovering pulps from teeth with more developed or complete roots (Perry et al., 2008; Takeda et al., 2008; Ducret et al., in press). Additionally, human dental pulp cells (HDPC) isolated at around the crown-completed stage displayed short cell doubling times and high growth rate (Takeda et al., 2008). We found similar results in our study. We also selected impacted teeth to minimize the risk of pulp tissue contamination and disease transmission by oral microorganisms (Nolla, 1960; Ducret et al., in press). This choice may enable to skip the step of sample disinfection performed

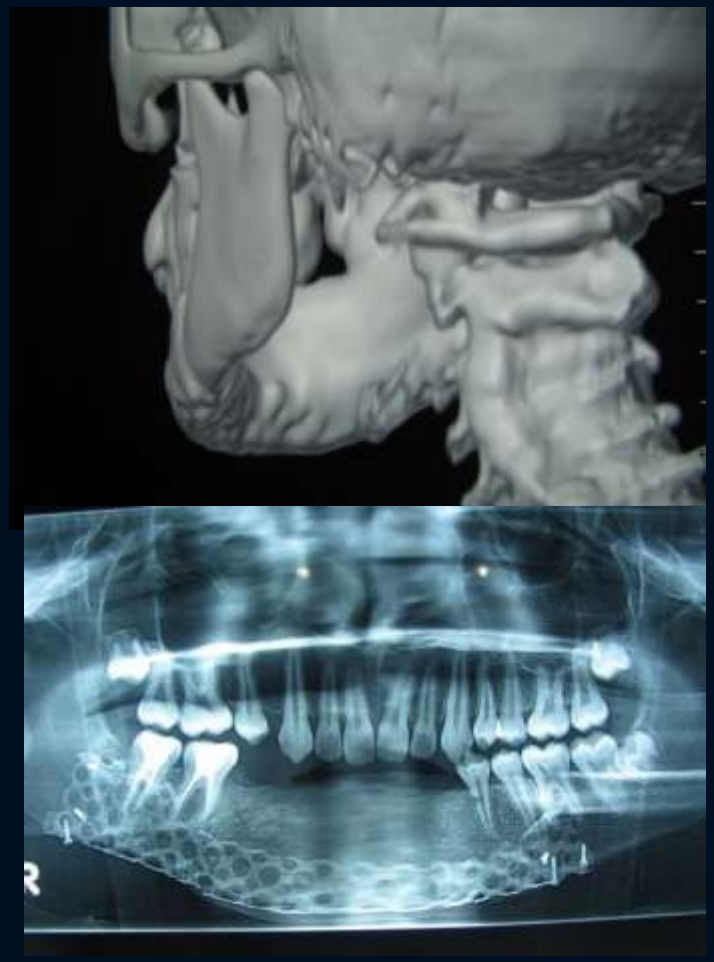
AMELOBLASOTOMA

AMELOBLASTOMA

Result

Pre OP

Post OP 6 Months



Post OP 4 Years

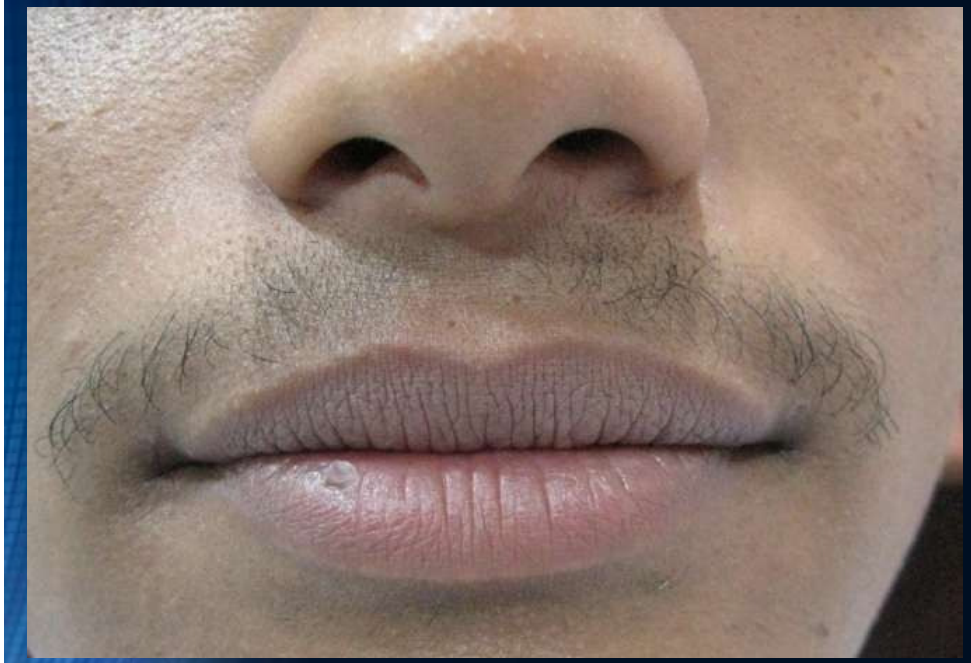
Image Source: Mothercell Regenerative Centre

www.mcrcindia.com

Regenerative & Aesthetic Medicine

Activated PRP for Hair Growth Stimulation

PRE OP



Injection Procedure

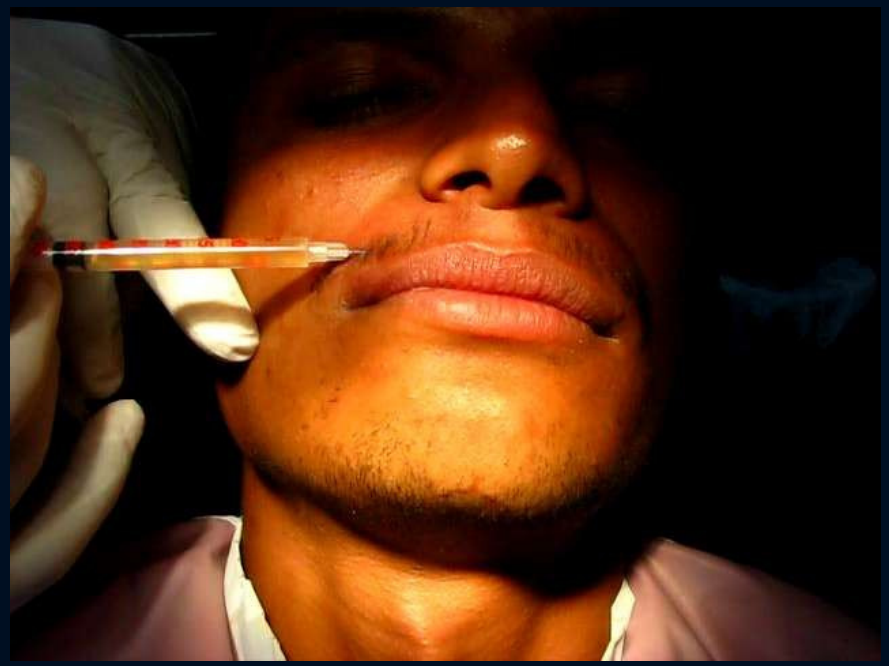
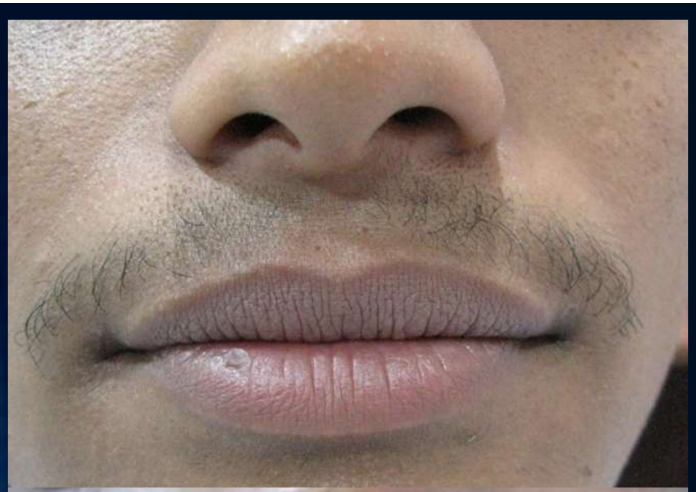


Image Source: Mothercell Regenerative Centre



PRE OP

AFTER 1st DOSE

AFTER 2nd DOSE

Image Source: Mothercell Regenerative Centre

References

1. Molavi, et al. (2016). Safety and Efficacy of Repeated Bone Marrow Mononuclear Cell Therapy in Patients with Critical Limb Ischemia in a Pilot Randomized Controlled Trial. Archives of Iranian medicine. 19. 388-396.

2. Kazuhisa Kondo et al. Long-Term Clinical Outcomes Survey of Bone Marrow-Derived Cell Therapy in Critical Limb Ischemia in Japan, Circulation Journal, 2018, Volume 82, Issue 4, Pages 1168-1178

3. Sankaranarayanan et al. Dental pulp stem cells for treating unhealed diabetic foot ulcer: a pioneering attempt. Journal of IDA TN. 2012; 4; 15

4. Ravi et al. Intra-articular injection of bone marrow concentrate protocol for Osteoarthritis – A preliminary report with 12 months follow up. Journal of Indian Orthopedic Rheumatology Association; January-June 2017:3(1);8-14. DOI: 10.18231/2455-6777 .2017.0002

5. Aristeidis et al. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. International Dental Journal 2018; 68: 22–30

6. Manimaran et al. Treatment of osteoradionecrosis of mandible with bone marrow concentrate and with dental pulp stem cells. Ann Maxillofac Surg. 2014 Jul-Dec; 4(2): 189–192. doi: 10.4103/2231-0746.147130

7. Ducret et al. Manufacturing of dental pulp cell-based products from human third molars: current strategies and future investigations. Front Physiol. 2015;6:213. Published 2015 Aug 6. doi:10.3389/fphys.2015.00213

8. Clinical Images – Speakers own cases at Mothercell Regenerative Centre, India