ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: 03/29/2016

ClinicalTrials.gov ID: NCT02727088

Study Identification

Unique Protocol ID:	P140941
Brief Title:	Pulpotomy vs Pulpectomy Outcome. (PULPSAVE)
Official Title:	Comparative Randomized Clinical Comparison of Pulp Chamber Pulpotomy and Root Canal Treatment (Pulpectomy) as a Permanent Endodontic Treatment of Mature Permanent Teeth: Analysis of Relationship Between Inflammation Biomarkers Pulpal Expression and Treatment Outcome
Secondary IDs:	IDRCB [2015-A01509-40]

Study Status

Record Verification:	February 2016
Overall Status:	Not yet recruiting
Study Start:	April 2016
Primary Completion:	April 2019 [Anticipated]
Study Completion:	April 2020 [Anticipated]

Sponsor/Collaborators

Sponsor:	Assistance Publique - Hôpitaux de Paris
Responsible Party:	Sponsor
Collaborators:	Rennes University Hospital Nantes University Hospital University Hospital, Clermont-Ferrand

Oversight

FDA Regulated?:	No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 2015/58 Board Name: CPP Ile de France IV Board Affiliation: French Health Authority Phone: 33(0)1 42 38 92 88 Email: cpp.iledefrance4@orange.fr
Data Monitoring?:	No
Plan to Share Data?:	No

Oversight Authorities: France: Ministry of Health

Study Description

Brief Summary: Epidemiological data show a significant rate of failure of endodontic treatment of 20 to 50% worldwide, probably directly related to the difficulty of the procedure. A successful pulpotomy allows the preservation of a vital radicular pulp into the root canal. The presence of a biological tissue into the root canal is definitely more efficient than a “complete” filling with an inert material. It has been shown on animal and human studies that this pulp stump in contact with the biomaterial is able to regenerate a dentinal plug, with the same architecture as physiologic dentin.

Primary objective : To compare the success rates of root canal treatment (reference) and conservative treatment (pulpotomy) for treating inflamed dental pulp on permanent mature teeth.

Secondary objectives : (1) To describe the clinical and biological prognostic factors of these two treatments; (2) to assess the additional value of biomarkers expression levels as a prognostic tool for clinical decision making (radical vs. conservative treatment); (3) to assess the impact of treatment on post-procedural pain.

This trial aims to demonstrate the non-inferiority of conservative pulpal treatment over endodontic treatment.

Patients consulting in one of the seven study centers, presenting one of the indications retained for the trial and giving written informed consent will receive the treatment (endodontic treatment or conservative treatment) allocated by randomization (stratified over the clinical diagnosis of the pulp status).

The follow up of patients include, a phone call at D15, and visit at 1, 6, 12 and 14 post operative months. Clinical examination and Xrays at 6, 12 and 24 months) will be used to evaluate the success or failure of the treatment.

During the treatment, a sample of pulp tissue will be withdrawn and transferred to a molecular biology laboratory for analysis of inflammation biomarkers. The aim of this part of the sudy is to assess a putative relationship (1) of regulation of biomarkers expression and clinical diagnosis, and (2) of regulation of these biomarkers and success rate of pulpotomy.

Success/failure evaluation:

The primary endpoint is the time to necessity of endodontic reintervention (analysed as a time to failure). This study will use an Intention To Treat analysis as its main assessment ; a secondary assessment accounting for peroperative conversions will assess the practical impact of these conversions. We will distinguish

- Direct failure (means that the failure is directly correlated to the treatment) : the reintervention need is due to the evolution of the treated tooth. This includes delayed onset of desmodontitis, periodontal space enlargement and/or periapical/ periradicular radiolucency (PAI>2) demonstrating an infection of the root canal system (filled by either pulpal stump or filling material).
- Indirect failure (means that the cause of the failure is not directly related to the endodontic treatment choice) : any event leading to endodontic reintervention indication NOT caused by radicular infection or restoration failure attributable to inadequate restoration. For example : new need of post-placement for treatment of loss of another tooth, unexpected progression of periodontal disease.

Both these failure modes are of interest for analysis : the direct failure time is an indication if the intrinsic value of a therapy, whereas the gross (direct+indirect) failure time is an indication of its clinical relevance (a good therapy applicable in rare cases may be less interesting than a mediocre but widely applicable one).

Statistical analysis:

The classical methods of descriptive analysis will be used to describe the raw results.

In order to make inferences directly on possible clinical results, this study will be analyzed in a Bayesian framework.

This study has been designed in reference with a frequentist demonstration of non-inferiority.

A non-inferiority trial with first and second species error rates α and β has the same operational characteristics as a superiority (unilateral trial) of error rates alpha and beta, which in turn needs the same study size as a comparison (=bilateral) trial with error rates α and 2β.

The final planned size of the trial is established as follows :

- Ideal plan : a nonparametric comparison (logrank test) fulfilling these goals according to this plan needs 158 patients overall under “perfect information” assumptions (no loss to follow-up, single analysis)
- Loss to follow-up : the expected loss to follow-up will cause about 22% of included patients to drop out of the study before final analysis this leads to include 194 patients overall.

Sequential analysis : since we wish to be able to follow the progress of the study, and to interrupt it if the main goal is reached, we choose to use a sequential analysis. A Pocock scheme needs to increase the sample size by 16% , leading to plan to recruit 226 patients overall.

Detailed Description: The accepted management for any pulpal intervention on a vital dental pulp is the pulpectomy (ablation of the whole dental pulp, preparation and filling of the whole root canal system, which is difficult and invasive). However, it has been shown that radicular pulp has a reparative potential and interesting immune defence properties. A pulp chamber pulpotomy (ablation of the coronal part of the pulp, easier and less invasive) may therefore be a better alternative. Its feasibility, known on decidual and immature permanent teeth (where it is a routine treatment) has been shown on mature permanent teeth. We aim to prove its non-inferiority to pulpectomy and study its prognostic factors.

Primary objective and primary endpoint:

To compare the success rates of root canal treatment (i.e. pulpectomy, reference treatment) and conservative treatment (pulpotomy) for treating dental pulpal inflammatory disease on permanent teeth, assessed by time to indication of re-treatment (time-to-failure) (primary endpoint). The investigator in charge of the patient proposes a classification of the failure, which must be validated by an adjudication committee.

Secondary objectives and endpoints:

1. To assess the impact of treatment on post-procedural pain;
2. To describe the clinical prognostic factors of these two treatments;
3. To assess the additional value of biomarkers expression levels as a prognostic tool for clinical decision making (pulpectomy vs. pulpotomy).

Study design:

Prospective, comparative, randomized study (randomized clinical trial)

Study population:

Adult patients with indication of pulpal intervention on a permanent mature non-necrosed tooth.

Adjudication committee:

The adjudication committee will review the classification of the failure for each patient, on the basis of data and radiographs and if necessary will submit queries sent to

investigator. The adjudication committee will finally classify the failure as direct or indirect.

Sample size and Power consideration:

Maximum of 226 patients, based on analogy with frequentist analysis:

- non-inferiority study, α =0.05, 1- β =0.8;
- expected rate of failure in the control group: 10% /year;
- maximal inferiority margin: hazard ratio=2;
- two years of accrual, one year of follow-up;
- each patient is followed up to the end of study;
- expected loss to follow-up 10%/year:
- loss of power due to interval censorship of clinically silent failure: negligible;
- sequential analysis (Pocock scheme, final test with final critical p=0.03).

Statistical analysis:

Bayesian analysis, analogous to a frequentist non inferiority study (RRmin=2) with α=0.05 and β=0.2

Bayesian modelling of survival of retreatment indication-free, assessing:

- Intergroup differences (Cox proportional hazards model if applicable, parametric modelling otherwise)
- Covariates impact (regression models) Assessment of predictive values of (clinical and biological) covariates.

Conditions

Conditions: Inflammatory Pulp Diseases Related to Carious Teeth.

Keywords: Dental Pulp Disease
Endodontics
Pulp Capping
Pulpotomy
Pulpectomy

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: N/A

Intervention Model: Parallel Assignment

Number of Arms: 2

Masking: Open Label

Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Enrollment: 226 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Pulpectomy : root canal treatment Pulpectomy : ablation of the whole dental pulp, preparation and filling of the whole root canal system	Procedure/Surgery: Pulpectomy ablation of the whole dental pulp, preparation and filling of the whole root canal system

Arms	Assigned Interventions
	Other Names: • root canal treatment (reference treatment)
Experimental: Pulpotomy : Conservative pulp management Pulpotomy : ablation of the coronal part of the pulp	Procedure/Surgery: Pulpotomy Conservative pulp management (experimental treatment): ablation of the coronal part of the pulp

Outcome Measures

Primary Outcome Measure:

1. To compare the success rates of root canal treatment (pulpectomy, reference) and conservative treatment (pulpotomy)
   [Time Frame: up to M36] [Safety Issue: Yes]
   Time to treatment failure, as assessed by the existence of an indication of re-intervention (with or without contra-indication).

Secondary Outcome Measure:

2. To assess the impact of treatment on post-procedural pain
   [Time Frame: D7] [Safety Issue: No]
   Acute post-operative pain
3. To describe the clinical prognostic factors of these two treatments
   [Time Frame: baseline, M1, M6, M12, M24, M36 and time to re-treatment] [Safety Issue: No]
   Clinical and radiological signs such as pain, maxillary bone lesion, periodontal attachment loss, …
4. To assess the additional value of biomarkers expression levels as a prognostic tool for clinical decision making (pulpectomy vs. pulpotomy).
   [Time Frame: baseline] [Safety Issue: No]

Eligibility

Minimum Age: 18 Years

Maximum Age:

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria :

1. Adult patients (≥ 18 years old),
2. Signed a written informed consent,
3. Mature permanent teeth, presenting with either:
   a. any indication of pulpectomy on asymptomatic pulp,
   b. pulp exposure during treatment of deep caries,
   c. reversible and irreversible pulpitis.
4. Access to permanent restorative treatment in a reasonable delay (1 month) after treatment.
5. Patient has a health coverage (affiliation to social security system or similar, excluding AME (Aide Médicale d'Etat)

Non-inclusion criteria :

1. General:
   a. Patient deprived of liberty or under legal protection measure
   b. Pregnant or nursing (lactating) woman or who does not apply effective contraception during the study
   c. Impossible or dubious follow-up;

d. Any general contra-indication to endodontic procedures;
e. Compromised general prognosis;
f. Immunodeficiency;
g. Anticoagulant and/or antiplatelet drug therapy
h. Participation to another clinical trial (to be discussed with the other trial's investigators);
i. Impossible or dubious post-procedure restorative treatment.

2. Local (pertaining to the candidate tooth):

a. Compromised local prognosis (e. g. trauma, periodontal disease);
b. Treatment plan including avulsion;
c. Treatment plan including radicular post placement;
d. Internal or external root resorption;
e. Preoperative evidence of pulp necrosis;
f. Presence of pulp stones into the pulp chamber clearly visible on the preoperative radiography.

Extemporaneous exclusion criteria:

1. Peroperative clinical evidence of complete or partial pulp necrosis (in one root at least on multirooted teeth);
2. Impossibility to control haemorrhage of the pulp on one canal at least.

Contacts/Locations

Central Contact: Stéphane SIMON, DDS, Mphil, PhD
Telephone: 33142161497
Email: stephane.simon@aphp.fr

Central Contact Backup: Marjorie ZANINI, DDS
Telephone: 33142161014
Email: marjoriezanini@hotmail.fr

Study Officials: Stéphane SIMON, DDS, Mphil, PhD
Study Principal Investigator
Assistance Publique des hôpitaux de Paris

Locations: France
Hôpital Pitié Salpêtriere
Paris, France, 75651

References

Citations:

Links:

Study Data/Documents: