Relevance and importance of clinical endodontic research, with emphasis on outcome studies

Dag Ørstavik, Oslo, Norway

Brussels Dec 13, 2008
Research techniques

- Epidemiological: True
- Clinical: Probable
- In vivo: animal: Likely
- Ex vivo: Doable
- In vitro: Possible
- Laboratory: Technically possible
- Literature: Basic or done before
Overview

• What is clinical research?
• Relevance: Legal aspects, manufacturers’ claims
• Importance: Necessary for improvement
• The relative irrelevance of experience
• Use of microbial markers
• The need for scepticism along side with enthusiasm
Research

• Research is scientific or critical investigation aimed at discovering and interpreting facts.

• Research may use the scientific method, but need not do so.
Modern methodology

- Topic of interest
- Question
- Hypothesis
- Design
- Qualitative/quantitative answers
Examples by title

• 1965: Histologic study of 155 impacted teeth.

• 1985: A comparison of antimicrobial effects of calcium hydroxide and iodine-potassium iodide.

• 2008: Clinical and radiographic comparison of primary molars after formocresol and electrosurgical pulpotomy: a randomized clinical trial.

• 2008: Periapical radiographs overestimate root canal wall thickness during post space preparation.
Clinical studies: done at chairside

- **Diagnosis**
  - Xrays, pain

- **Treatment**
  - Prophylaxis, medicaments, materials, techniques

- **Disease**
  - Monitoring, criteria

- **Tooth survival**

JOE clinical section: Used to be any study which applied clinical techniques
Ex vivo

- From Wikipedia, the free encyclopedia
- *Ex vivo* (Latin: out of the living) means that which takes place outside an organism. In science, ex vivo refers to experimentation or measurements done in or on living tissue in an artificial environment outside the organism with the minimum alteration of the natural conditions.
In vitro

- From Wikipedia, the free encyclopedia

- *In vitro* (Latin for within the glass) refers to the technique of performing a given experiment in a controlled environment outside of a living organism; for example in a test tube. In vitro fertilization is a well-known example of this.
Technological experiments

• Physical testing:
  – Materials, techniques

• Chemical testing:
  – Composition, reactions

• Manipulative and functional tests:
  – Bench-top usage tests: working time, setting time, leakage (like ex vivo, but the process is lab defined)
Animal experiments

- Biological tests
  - Toxicity, allergenicity, inflammatory potential

- Usage tests
  - Medicaments and devices applied as suggested for human use
RESTORING OR MAINTAINING COMPLETE PERIAPICAL HEALTH
Endodontics is:

Prevention or treatment of apical periodontitis

which in practice means

*Protection against or elimination of root canal infection*

Diagnostics, choice of treatment method, irrigation, medication and root filling are all means towards this end

Ørstavik 1988
Choosing the relevant test

<table>
<thead>
<tr>
<th>Study target</th>
<th>Clinical</th>
<th>Laboratory</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotoxicity</td>
<td>-</td>
<td>+</td>
<td>++++</td>
</tr>
<tr>
<td>Biocompatibility</td>
<td>+/-</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Antibacterial</td>
<td>++++</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>Debris removal</td>
<td>+</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Leakage</td>
<td>++++</td>
<td>++++</td>
<td>+/-</td>
</tr>
<tr>
<td>Disease</td>
<td>++++</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Tooth survival</td>
<td>++++</td>
<td>++</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Endodontics is:

Prevention or treatment of apical periodontitis

Ørstavik 1988
Eriksen 1998

- Remaining teeth, no.
- Root-filled teeth, %
- Apical periodontitis, %
Fig. 6. The prevalence of apical periodontitis in different populations.

Results of endodontic treatment based on the presence of apical periodontitis associated with root-filled teeth evaluated from radiographs.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Avg age</th>
<th>Succ</th>
<th>Fail</th>
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<tbody>
<tr>
<td>Eriksen and Bjertness 1991 (Norway)</td>
<td>50</td>
<td>64</td>
<td>36</td>
</tr>
<tr>
<td>Ödesjö et al. 1990 (Sweden)</td>
<td>45</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>Imfeld 1991 (Switzerland)</td>
<td>66</td>
<td>69</td>
<td>31</td>
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<tr>
<td>de Cleen et al. 1993 (the Netherlands)</td>
<td>38</td>
<td>61</td>
<td>39</td>
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<tr>
<td>Buckley and Spångberg 1995 (USA)</td>
<td>45</td>
<td>69</td>
<td>31</td>
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<tr>
<td>Ray and Trope 1995 (USA)</td>
<td></td>
<td>61</td>
<td>39</td>
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<tr>
<td>Saunders et al. 1997 (Scotland)</td>
<td>(20-60+)</td>
<td>42</td>
<td>58</td>
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<tr>
<td>Weiger et al. 1997 (Germany)</td>
<td></td>
<td>39</td>
<td>61</td>
</tr>
<tr>
<td>Marques MD et al. 1998 (Portugal)</td>
<td>35</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>Georgopoulou MK et al. 2005 (Greece)</td>
<td>48</td>
<td>40</td>
<td>60</td>
</tr>
</tbody>
</table>

| Mean value                                    | 45      | 63   | 37   |
| "Success range"                               |         | 39-78 % |

From: Harald Eriksen 2008 In: Ørstavik & Pitt Ford, *Essential Endodontology*
Factors known to affect the prognosis of "endodontic treatment"

- Cotton TP, Schindler WG, Schwartz SA, Watson WR, Hargreaves KM.

A retrospective study comparing clinical outcomes after obturation with Resilon/Epiphany or Gutta-Percha/Kerr sealer. (endodontist, recalled at 2–25 months)

Factors known to affect the prognosis of "endodontic treatment"

- Gender .06† Males worse
- Appointments .06† Multiple worse
- Pulp diagnosis .001† Nonvital worse
- Preoperative lesion .003† Present worse
- No. of canals obturated 1†
- Recall time .68†
- Age .25
- Tooth position .26†
- Obturation material 1†
Factors known to affect the prognosis of "endodontic treatment"


<table>
<thead>
<tr>
<th>Obturation material, n (%)</th>
<th>Healed</th>
<th>Nonhealed</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resilon</td>
<td>42 (79.2)</td>
<td>11 (20.8)</td>
<td>43 (100)</td>
<td>1†</td>
</tr>
<tr>
<td>Gutta-percha</td>
<td>39 (78.0)</td>
<td>11 (22.0)</td>
<td>50 (100)</td>
<td></td>
</tr>
<tr>
<td>Total (some w no pulp Dx)</td>
<td>81</td>
<td>22</td>
<td>103</td>
<td></td>
</tr>
</tbody>
</table>
Factors known to affect the prognosis of "endodontic treatment"


<table>
<thead>
<tr>
<th>Preoperative lesion, n (%), p Value</th>
<th>Healed</th>
<th>Nonhealed</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>43 (66.2)</td>
<td>22 (33.8)</td>
<td>65 (100)</td>
<td>&lt;.001†</td>
</tr>
<tr>
<td>No</td>
<td>38 (100)</td>
<td>0 (0.0)</td>
<td>38 (100)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>81</td>
<td>22</td>
<td>103</td>
<td></td>
</tr>
</tbody>
</table>
Prognosis for Pulpectomy: Prevention of Apical Periodontitis

- Strindberg 1956 94
- Kerekes & Tronstad 1979 97
- Sjögren et al 1990 97
- Marquis et al 2006 93

- This is probably a reflection of an almost complete success – failures are iatrogenic, via contamination, and avoidable.
Prognosis for Root Canal Infection: Treatment of Apical Periodontitis

- Strindberg 1956 88
- Kerekes & Tronstad 1979 91
- Sjögren et al 1990 86
- Marquis et al 2006 80
- Zmener & Pamejer 2004 89

- This is probably a reflection of persistent infection – failures are due to inadequate disinfection
Bacteriology and the prognosis of "endodontic treatment"

• …When no bacteria remained [in the root canal before filling], healing occurred independently of the quality of the root filling. In contrast, when bacteria remained, there was a greater correlation with non-healing in poor-quality root fillings than in technically well-performed fillings. …..

• How well do we do?

The prognosis

• All teeth, the real world: 67%
• Follow-up of vital teeth with root filling 95%
• Follow-up of infected teeth treated with root filling 85%
• Follow-up of conservative revision 70%
• 40/40/20 in your practice? ?%
• How well do we do?
The prognosis

• All teeth, the real world: 67%
• Follow-up of vital teeth with root filling 95%
• Follow-up of infected teeth treated with root filling 85%
• Follow-up of conservative revision 70%
• 40/40/20 in your practice? 86%
• How well do we do?
What lies behind the finding that every third root filled tooth has apical periodontitis?
The incidence of healing after treatment of apical periodontitis may be alarmingly low

<table>
<thead>
<tr>
<th>Pre-op Dx</th>
<th>Nos.</th>
<th>Success rates</th>
<th>Prop's</th>
<th>n</th>
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<tr>
<td>'vital'</td>
<td>50</td>
<td>'vital' s rate</td>
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<td>10</td>
<td>'vital' s rate</td>
<td></td>
<td>9</td>
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<tr>
<td>'infected', lesion</td>
<td>30</td>
<td>'necrotic' s rate</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>'revision, infected'</td>
<td>10</td>
<td>'necrotic' s rate</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>overall s rate</td>
<td></td>
<td>67</td>
</tr>
</tbody>
</table>
Radiographic evaluation and follow-up: hows and whys

• This part is a review of
  – Different methods of radiographic follow-up methods
  – The strengths and limitations of assessment of one’s own cases
  – Clinical-radiographic testing of medicaments, materials and techniques
<table>
<thead>
<tr>
<th>Pre-op Dx</th>
<th>Case s</th>
<th>Success rates s</th>
<th>Prop' n</th>
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</thead>
<tbody>
<tr>
<td>'vital'</td>
<td>50</td>
<td>'vital' s rate</td>
<td>0.75</td>
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<tr>
<td>'necrotic'</td>
<td>10</td>
<td>'vital' s rate</td>
<td>0.75</td>
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<tr>
<td>'infected'</td>
<td>20</td>
<td>'necrotic' s rate</td>
<td>0.55</td>
</tr>
<tr>
<td>'revision, infected'</td>
<td>20</td>
<td>'necrotic' s rate</td>
<td>0.55</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>overall s rate</td>
<td>0.67</td>
</tr>
<tr>
<td>Pre-op Dx</td>
<td>Cases</td>
<td>Success rates</td>
<td>Prop's</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------</td>
<td>---------------</td>
<td>--------</td>
</tr>
<tr>
<td>'vital'</td>
<td>10</td>
<td>'vital' s rate</td>
<td>0.95</td>
</tr>
<tr>
<td>'necrotic'</td>
<td>10</td>
<td>'vital' s rate</td>
<td>0.95</td>
</tr>
<tr>
<td>'infected'</td>
<td>20</td>
<td>'necrotic' s rate</td>
<td>0.70</td>
</tr>
<tr>
<td>'revision, infected'</td>
<td>20</td>
<td>'necrotic' s rate</td>
<td>0.70</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>overall s rate</td>
<td>0.78</td>
</tr>
</tbody>
</table>
Elements in endodontic follow-up studies

• Outcome parameters
  success/failure, healing, survival; other

• Study design
  pro- & retro; power (β); randomization;

• Operator performance: Art, science and reality: the possible, best average and likely outcome
Art

The case report: See what I can do, by listening, you share the glory

From Visual Endodontics
Best average

Typically institutional or specialist practice follow-up studies; the self-assured clinician comfortably states, ”We have more than a 90 per cent success rate!”
Real average?

Cross-sectional, epidemiological approaches: the whole range; nobody wants to be associated with this.
Different situations of radiographic follow-up methods

• Case-by-case monitoring for healing or emergence of apical periodontitis: everyday practice

• Particular clinical situations: eg, perforations, apexification, cyst size reduction: practice and case reports

• *Feasibility* studies: case series

• Scientific clinical studies: influence of specific clinical/biological/technical variables
How do we do: the evidence ladder

- High-quality systematic reviews
- Large randomized trials with clear-cut results
- Small randomized trials with uncertain results (i.e., positive trends without statistical significance)
- Nonrandomized trials with contemporary controls
- Nonrandomized trials with historical controls
- Cohort studies: one population over time
- Case-control studies: retrospective, analysis of factors (typical follow-up)
- Dramatic results from uncontrolled studies (e.g., the treatment of infections with penicillin in the 1940s)
- Case series and other descriptive studies
- Reports of expert committees and opinions of respected authorities, based on clinical experience

Sutherland J Can Dent Assoc 2001; 67:375-8
<table>
<thead>
<tr>
<th>Level</th>
<th>Therapy/Prevention, Aetiology/Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Systematic Review (with homogeneity) of Randomized Clinical Trials</td>
</tr>
<tr>
<td>1b</td>
<td>Individual Randomized Clinical Trials (with narrow Confidence Interval)</td>
</tr>
<tr>
<td>2b</td>
<td>Individual cohort study (including low quality RCT; e.g., &lt;80% follow-up)</td>
</tr>
<tr>
<td>3a</td>
<td>Systematic Review (with homogeneity) of case-control studies</td>
</tr>
<tr>
<td>3b</td>
<td>Individual Case-Control Study (few cases, matching controls)</td>
</tr>
<tr>
<td>4</td>
<td>Case-series (and poor quality cohort and case-control studies)</td>
</tr>
<tr>
<td>5</td>
<td>Expert opinion without explicit critical appraisal, or based on physiology, bench research or &quot;first principles&quot; (logical deduction)</td>
</tr>
</tbody>
</table>

The single case report: A valuable contribution to the scientific literature

Gould 3xO September 2001 editorial

• "I wish to advocate for the validity and value of the single case report. I believe that the case report with appropriate content remains an important contribution to the body of clinical and diagnostic information for oral health care providers and researchers."
The single case report:
The demands of and insights from treatment of the tooth/individual combination

- What do you do when you have ”tried it all” and it does not work?
- You discuss with your patient and apply a treatment suggested or untried, but doing no inherent harm
- Dentistry is seldom life-threatening
Different methods of radiographic follow-up methods

- Success-failure analysis
- Probability assessments
- Lesion size monitoring
- The PAI scoring system
- Quantitative methods
- New radiographic techniques
Case monitoring for healing or retreatment

• Simple "success/failure"-analysis in practice
  – AP development
  – AP resolution

• Yes or no with time & subject variation
Vital Infected pulp; apical periodontitis

Instrumentation & irrigation

Dressing

Filled & healing

Complete healing

Root canal infection

Time

Root canal infection
• success when
  – a, the contours, width and structure of the periodontal margin were normal
  – b, the periodontal contours were widened mainly around the excess filling

• failure when there was
  – a) a decrease in the periradicular rarefaction
  – b) an unchanged periradicular rarefaction
  – c) an appearance of new rarefaction or an increase in the initial

• uncertain when
  – a) there were ambiguous or technically unsatisfactory control radiographs which could not for some reason be repeated
  – b) the tooth was extracted prior to the 3-year follow-up owing to the unsuccessful treatment of another root of the tooth
Probability assessments

• Definitively no disease 1
• Probably no disease 2
• Uncertain 3
• Probably disease 4
• Definitively disease 5
Probability assessments

Advantages: numerical, reflects subjective variation in diagnosis
## Probability assessments

<table>
<thead>
<tr>
<th>Score</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
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<tbody>
<tr>
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<td>16</td>
<td>5</td>
<td>1</td>
<td>7</td>
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<td>24</td>
<td>21</td>
<td>18</td>
<td>21</td>
<td>25</td>
</tr>
</tbody>
</table>

Ørstavik et al 1986
Lesion size monitoring

- Quantitative
- Numerical, continuous scale
- Reflecting the biological process?
Lesion size monitoring

Lesions may not develop as balloons growing or heal by apposition from within the shell of the bony lesion.

ImageJ

From Friedman et al 1997
Scoring Systems in Clinical Dentistry

- Caries
Scoring Systems in Clinical Dentistry

- *Caries*: limited progress until DMF index was established (1938)
  - Epidemiology
  - Cohort studies
  - Fluoride
  - Local and topical agents
  - Public health monitoring
Scoring Systems in Clinical Dentistry

- **Caries**: limited progress until DMF index was established (1938)
- **Gingivitis & marginal periodontitis**
Scoring Systems in Clinical Dentistry

• *Caries*: limited progress until DMF index was established (1938)

• *Gingivitis & marginal periodontitis*: confusion until indices were applied (1950-60)
Scoring Systems in Clinical Dentistry

- **Caries:** limited progress until DMF index was established (1938)
- **Gingivitis & marginal periodontitis:** confusion until indices were applied (1950-60)
- **Apical periodontitis (pulpitis)?**
Scoring Systems in Clinical Dentistry

• *Caries*: limited progress until DMF index was established (1938)

• *Gingivitis & marginal periodontitis*: confusion until indices were applied (1950-60)

• *Apical periodontitis*: Calibrated indices? X-ray digitized measurements?
The PAI Scoring System

• Apical periodontitis: A calibrated index

Ørstavik et al. 1986: The periapical index: a scoring system for radiographic assessment of apical periodontitis
Brynolf 1967: A histological and radiological study of the periapical region of human upper central incisors

300 teeth with histology and radiographs
Brynolf 1967: A histological and radiological study of the periapical region of human upper central incisors

Ørstavik et al. 1986: The periapical index: a scoring system for radiographic assessment of apical periodontitis

Seven histologic/radiographic groups

Five radiographic categories on an ordinal scale of severity
The PAI scoring system is a radiographic interpretation on a 5 point scale from 1-5 in order of absence to presence and increasing severity of disease.

*It uses a reference set of radiographs with corresponding line drawings and their associated score on a photographic print or computer screen.

*The scores are based on a correlation with inflammatory periapical status confirmed by histology.
Nine radiographs from Brynolf's selection were taken as representatives of the five categories, verbally described as:

1 - Normal apical periodontium
2 - Structural changes in periapical bone
3 - Structural changes with mineral loss
4 - Overt radiolucency
5 - Structural changes peripheral to radiolucency
• Find the reference radiograph where the periapical area most closely resembles the periapical area you are studying. Assign the corresponding score to the observed root.

• When in doubt, assign a higher score.

• For multirooted teeth, use the highest of the scores given to the individual roots.

• All teeth must be given a score.
Calibration

- **Material:**
- Reference scale
- Set of written instructions for scoring
- Set of 100 radiographs, one tooth in each is scored. The 'true scores' have been determined by consensus of two endodontists involved with the development of the system.
- Excel file for computation of essential statistical parameters.
Calibration

• **Procedure:**

  • Day 1: Scoring of the 100 X-rays producing scoring set 1. Discussion of results in comparison with 'true scores'. Emphasis is placed on scores deviating more than 1 unit from the 'true scores'.

  • Day 2. Repetition of day 1 with production of scoring set 2.

  • Day 5. Repetition of day 1 with production of scoring set 3.

  • Calculation of kappa. \( K > 0.61 \) and higher is acceptable. An observer with kappa values for inter- and intra-observer reproducibility of \( >0.61 \) is 'authorised' to produce valid experimental scores.

  • 20+ observers world-wide calibrated; i.e., they judge populations of teeth similarly/identically.
The ridit statistic

Parametric statistics
Change of PAI in cases with bacteria absent or present at the second appointment. Single visit cases are not included.

Usage

- 16 countries
- 40+ publications
- Retrospective clinical follow-ups
- Epidemiological studies
- Prospective studies
Weaknesses of the PAI system

- Front tooth reference only
- Moderate specificity
Radiographic follow-up after endodontic treatment
S. Huumonen & D. Ørstavik, in prep.

• Aim

– To assess radiographically the rate and pattern of healing apical periodontitis after endodontic treatment. Furthermore healing of different tooth types was analysed.
Radiographic follow-up after endodontic treatment
S. Huumonen & D. Ørstavik, in prep.

• Methodology

  - Radiographic data from 7 prospective clinical studies was pooled to get large material for analysis. A total of 1410 teeth were included into the analysis. The periapical status was evaluated using the Periapical Scoring System (PAI). The total follow-up period was 4 years, with intervals varying between controls from 3 months to a year.
• Results

  - Significant healing of apical periodontitis was evident at 3 months, and 27% of treated teeth were considered healthy at this early time point. At one year the proportion of completely healed teeth had increased to 41%. Thereafter, healing continued more slowly. Upper lateral incisors were overrepresented among teeth with apical periodontitis which did not show healing within one year postoperatively.
Periapical changes after treatment

% healthy, PAI=1-2

Time, WEEKS

Start PAI

- PAI 1
- PAI 2
- PAI 3
- PAI 4
- PAI 5
Radiographic follow-up after endodontic treatment
S. Huumonen & D. Ørstavik, in prep.

• Conclusion

– Significant healing of apical periodontitis was seen at 3 months postoperatively.

– Approximately half of teeth were healed within the first year.

– Improvement of periapical status was slower in PAI groups 4 and 5 compared with PAI 3 during the first year.

– After two years, improvement of periapical status continued similarly among different preoperative apical periodontitis groups of teeth.

– Upper lateral incisors failed to heal more often than other tooth types.
Apical surgery

- Healing of periodontitis
- Healing of operation wound
- No histological correlate
After Molven et al. 1987: a visual, not verbal reference is used
After Molven et al. 1987
After Molven et al. 1987
Results of endodontic retreatment: a randomized clinical study comparing surgical and nonsurgical procedures.


- Conclusively, this study failed to show any systematic difference in the outcome of surgical and nonsurgical endodontic retreatment. Surgical retreatment seems to result in more rapid periapical bone fill, but also may imply a higher risk of "late failures." From a scientific point of view, the length of the follow-up period is very important and may strongly influence the conclusions made.
Results of endodontic retreatment: a randomized clinical study comparing surgical and nonsurgical procedures.
Endodontic surgery with and without inserts of bioactive glass PerioGlas(R)-a clinical and radiographic follow-up.


Pantchev A, Nohlert E, Tegelberg A.

OBJECTIVE: This study evaluated the use of bioactive glass, PerioGlas(R), after retrograde filling with Super EBA cement in the treatment of periapical bone destruction. STUDY DESIGN: Healing outcomes were followed up after endodontic surgery in 186 teeth. Outcomes were divided into two groups according to follow-up time: short- and long-term. The EBA group (n = 110) underwent endodontic surgery and retrograde filling with EBA cement. In the EBA + PerioGlas(R) group (n = 76), PerioGlas(R) was embedded in the bone cavity after retrograde filling.
Endodontic surgery with and without inserts of bioactive glass PerioGlas(R)-a clinical and radiographic follow-up.


Pantchev A, Nohlert E, Tegelberg A.

RESULTS: The success rate in the EBA + PerioGlas(R) group was 72% compared with 56% in the Super EBA group at the short-term follow-up and 74% and 84%, respectively, at the long-term follow-up. Healing of periapical bone destruction classified as uncertain at the short-term follow-up was considered successful in two out of three cases at the long-term follow-up.
Endodontic surgery with and without inserts of bioactive glass PerioGlas(R)-a clinical and radiographic follow-up.

**CONCLUSION**: This study found that PerioGlas(R) as bone substitute did not significantly improve endodontic healing outcome.
PerioGlas: PubMed

- Bioactive glass: 989 articles
- PerioGlas: 481 articles
- PerioGlas surgery: 211 articles
- PerioGlas endodontic: 4 articles
Digital manipulation
Ratio method

X-ray healing

Digital change

AP/N < 1

AP/N ≅ 1

Ap/N < 1 Ap/N ≅ 1
Numbers are average gray values in the defined areas: 255=white; 0=black

Digital change

AP/N = 0.62  →  AP/N 0.88
Other methods:
- digital subtraction
- visual enhancement
Scintigraphy and digital manipulation: Fine for visualization, so far no application in quantitative approaches

Huumonen & Orstavik 2002
CT: Fine for visualization, so far no application in quantitative approaches

Huumonen & Orstavik 2002
Feasibility studies

• These are basically case series documenting that a given technique, material or medicament may be used with a fair expectation of success (Endorez, Resilon)
Glass ionomer sealer

Of 378 followed-up teeth, there was 78.3% success, 15.6% incomplete healing, and 6.1% failure.

Harmonized criteria? Reproducibility?

Friedman et al., 1995
Clinical Study – EndoRez

Zmener O, Pameijer CH. 2004

'Feasibility study'
Resilon - Epiphany

Of 38 teeth with an initial PAI score of $\geq 3$, 58% had a PAI score $\leq 2$ after 12 months.

Heffernan et al., 2006
Resilon - Epiphany

Of 38 teeth with an initial PAI score of $\geq 3$, 58% had a PAI score $\leq 2$ after 12 months.

Harmonized PAI scores make all the difference

Trope et al: ca. 75 %; Huumonen & Ørstavik: ca: 50 %

Heffernan et al., 2006
Conclusions on case series

• Valuable baseline for general acceptance of a product or method

• No comparison with other products unless Tx and analysis methods are standardized:
  – Nonrandomized trials with historical controls are then OK
Particular clinical situations

• Perforations, fractures, open apices, endo-perio, differential diagnosis may represent problems that have unique radiographic features and must be separated from follow-up analyses.
Scientific clinical studies

• Defined criteria for outcome parameters including
  – Subjective symptoms
  – Objective symptoms
  – Radiographic characteristics
  – Temporal aspects
• Systematic discrimination of variables
• Retro- or prospective
• Randomized distribution and unbiased evaluation
Assessment of one’s own cases

• Careful selection of cases for systematic studies:
  – Preoperative diagnosis
  – Complications
  – Technically difficult cases
  – Surgical variables, if applicable

• Limitations of one’s own long-term follow-up experiences
Self-assessment

• Suppose 200 patients are seen for control each year,
• this gives a 95% confidence interval for success rates around 85% of
• 80 to 90%
• i.e., there is no way anyone can register a real change in treatment outcome of less than some 10%!
Self-assessment: example

• For detail, suppose that of the 200 patients, perhaps 80 had CAP,

• of which at least ¼ had to be treated in 2 or more appointments anyway, leaving 60,

• which gives a conf int of 76 to 94%

• i.e., there is no way anyone can register a real change in therapeutic outcome of less than some 20%
’It works in my hands’: How many cases do you really need to document a difference in performance?
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Old method</th>
<th>New method</th>
<th>Success %</th>
<th>Success</th>
<th>Failure</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Success</td>
<td>85</td>
<td>94</td>
<td>89,5</td>
<td>85</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>Failure</td>
<td>15</td>
<td>6</td>
<td>10,5</td>
<td>15</td>
<td>6</td>
<td>10,5</td>
</tr>
</tbody>
</table>

Chi-square value: 4,3096568
Degrees of freedom: 1

Success %

Chi-square value: 3,84
Degrees of freedom: 1
Even 200 cases are not very discriminating: How many cases do you follow up systematically?

And who controlled and randomized the variables influencing bacteria in the canal, or other variables affecting the final outcome?
Finally: any new method or new material is correctly applied to simple cases first, recognizing the learning curve. When such cases are retrospectively assessed, they should have a better outcome than the average or complicated case.
Assessment of one’s own cases

- There are serious limitations just by the numbers needed, in one’s own ability to assess outcome
- Base-line harmonization almost impossible and
- Case selection crucial
- But: the unusual case is still evading systematic studies, and treatment will still have to be based on hearsay: cf the plea for the case report
Conclusions from theoretical considerations

• Sharing practice experiences is an inadequate method of improving performance

• *Systematic improvements must rely on well-designed clinical studies*

• First: do we really need improvement?
Clinical testing of medicaments, materials and techniques

• Traditional feasibility tests
• Analysis of retrospective testing
• Prospective studies; comparison with historical data
• Randomized, controlled clinical studies
Clinical Evaluation

• Prevention

  – failure: AP developing where none existed

  – AH26 vs ProcoSol (Grossman’s sealer) vs Kloroperka: Significantly poorer results for Kloroperka in one clinical study
Cumulative PAI Scores

AH  KP  PS

TIME: 0 to 4 years

Ørstavik et al., 1986
Numbers are average gray values in the defined areas: 255=white; 0=black

$AP/N = 0.62$  $\rightarrow$  $AP/N 0.88$

Digital change
Healing by AP/N Ratio

PA Status, P/N ratio

TIME, weeks

PS
SA
Healing by PAI Score

TIME, weeks

PA Status, PAI ridit

PS
SA
Single-visit: both PAI score and ratio method

From Trope et al., 1998
<table>
<thead>
<tr>
<th>TX</th>
<th>N</th>
<th>Ratio average gray value on original image at 52 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>23</td>
<td>0.9897</td>
</tr>
<tr>
<td>E</td>
<td>21</td>
<td>0.9279</td>
</tr>
<tr>
<td>O</td>
<td>41</td>
<td>0.9555</td>
</tr>
</tbody>
</table>

Delano et al 2001
The effect of the sealer used on changes in periapical status (The boxes show the 1st and 3rd quartiles with the median value in bold line. The whiskers show the minimum and maximum). Identical letters indicate no statistically significant differences ($\alpha = 0.01$).
Preoperative Healthy Periodontium: Effect of Sealer

From Waltimo et al 2003

Range of s.e. of means: 0.03-0.17
Healing of apical periodontitis following root filling with 3 different sealers

From Waltimo et al 2003

Range of s.e. of means: 0.02-0.07
Preoperative Healthy Periodontium: Effect of an Adhesive, Seal-Tight Sealer?

![Graph showing the effect of different adhesives on periapical status over time.](image)

- **Total**
- **ProcoSol**
- **Sealapex**
- **CRCS**
- **Best possible**
- **Still good**

Range of s.e. of means: 0.03-0.17

From Waltimo et al. 2003
Comparative clinical testing

• ProcoSol, Grossman’s sealer: reference
  – AH26: as good or better
  – Sealapex: as good or better
  – CRCS: no worse
  – RoekoSeal no worse
  – GuttaFlow no worse
  – Kloroperka poorer
  – Epiphany as good or better

• Lateral condensation reference:
  – Warm vertical as good or better
The one-step issue

Courtesy E Elkjaer
Periapical improvement with time

PAI 3-5 at start

Trope et al 1999
Calcium hydroxide was placed in the instrumented root canals of 31 teeth for at least one week and the treatment finished at the second visit. Thirty-six teeth were root canal treated at one visit. .... a follow-up time of 4.5 years.

Weiger et al., Calcium hydroxide and prognosis of RCT. IEJ 2000; 33:219-226
• **Methodology** Thirty-nine patients received root-canal treatment. In the first visit, teeth were instrumented, and 18 of these teeth were filled (after microbiological sampling) with calcium hydroxide in sterile saline. The other 21 teeth were obturated with gutta-percha and AH-26 sealer after microbiological sampling. Four weeks later, the teeth with calcium hydroxide were accessed again and after microbiological sampling they were obturated with gutta-percha and AH-26 sealer. Healing of periapical radiolucency was recorded over a period up to 4.5 years.
18 teeth were filled with calcium hydroxide ...
The other 21 teeth were obturated with gutta-percha and AH-26 sealer. Four weeks later, the teeth with calcium hydroxide were ... obturated with gutta-percha and AH-26 sealer.
Conclusions:
Trope et al. 1999

• …. the calcium hydroxide group showed the most improvement in PAI score .. followed by the one-step group (74% vs. 64%). ….. it was shown that large experimental groups on the order of hundreds of patients would be required to show significant differences.
Conclusions: Weiger et al. 2000

• …. one-visit root canal treatment created favourable environmental conditions for periapical repair similar to the two-visit therapy when calcium hydroxide was used as antimicrobial dressing. One-visit root canal treatment is an acceptable alternative to two-visit treatment for pulpless teeth associated with an endodontically induced lesion.

• … no significant differences in healing of periapical radiolucency was observed between teeth that were treated in one visit (without) and two visits with inclusion of calcium hydroxide for 4 weeks. The presence of a positive bacterial culture (CFU<10²) at the time of filling did not influence the outcome of treatment.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Risk difference (%)</th>
<th>95% CI</th>
<th>Weight (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trope et al. (1999)</td>
<td>10</td>
<td>-18.2 to 38.3</td>
<td>48.25 (24.8)</td>
<td>0.491</td>
</tr>
<tr>
<td>Weiger et al. (2000)</td>
<td>-12.4</td>
<td>-32.5 to 7.7</td>
<td>95.20 (49)</td>
<td>0.226</td>
</tr>
<tr>
<td>Peters &amp; Wesselink (2002)</td>
<td>-10.4</td>
<td>-37.8 to 17</td>
<td>51.14 (26.2)</td>
<td>0.455</td>
</tr>
<tr>
<td>Combined three studies</td>
<td>-6.3</td>
<td>-20.3 to 7.8</td>
<td>NA</td>
<td>0.381</td>
</tr>
</tbody>
</table>

Negative value indicates the difference is in favour of single-visit endodontics. NA, not applicable.
Arguments

• Disease diagnosis is the critical entity in outcome/follow-up studies

• We need improved registrations of disease, primarily in conventional, clinical-radiographic follow-up studies

• We need extended cooperation in clinical research in endodontontology: to acquire the numbers needed, multicenter studies with uniform recordings are needed
Future Improvements and Shortcuts

- Quantitative, digital analysis – qualified success
- Computerized tomography – still limited by the dose involved
- Relationship of long-term to short-term outcome results
- Relationship to other clinical parameters
  - Serum markers
  - Microbial markers
Instrumentation

- Length: epidemiology: root filling length a measure of instrumentation length
- Shape: taper; retention of canal shape
- Width: bacteriology
End point of root filling and success

Ketterl 1965
Aspects of instrumentation

No preoperative apical perio: Instrumentation length/overfilling of little importance

Sjögren et al. 1991
Distribution of end points of root fillings

A: Dental School I; B: Dental School II; C: Endodontist Private Practice. N > 100
Suppose we get there – how well do we clean?
Effectiveness of three instrumentation systems in the cleaning of root canals

Appelstein et al. JOE April 2003, OR 17

![Cleaning of root canals graph]

- **Debris index**
- **Root level**
  - Coronal
  - Middle
  - Apical

- **Cleaning of root canals**
  - Stainless steel K files
  - ProFile
  - Race
Bacteriological effects

The qualitative aspect of bacteriological sampling is becoming increasingly sophisticated, with gene technology and analyses also being used for identification of bacteria in the root canal.

The problem of representativity of sampling remains, however.
Use of microbial markers

- Endodontics is the prevention or treatment of apical periodontitis
- Apical perio is caused by microbial infection of the root canal system
- Presence of cultivable bacteria at the time of filling is directly associated with the probability of healing
- Can we use microbial sampling as a tool predicting long-term outcome?
Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis.

Sjögren et al. 1997

Chemomechanical preparation, one visit

S1: 40% positive teeth

Root-filling

5 year Follow up

7 failed 15 healed

68% success rate

P<0.05

55 infected teeth

22 with bacteria

31 bacteria free

29 healed 2 failed

94% success rate
Bacteriological sampling procedures: Complete vs. discrete
Growth after extensive reaming: a clinical pilot

Sample
A  On admission
D1  First reamer to bite
D2  Final reamer, complete apical circle
R1  Second appointment, next reamer up

Ørstavik et al. 1991
Growth after extensive reaming: log10 values

Ørstavik et al. 1991
Growth after extensive reaming: log10 values

<table>
<thead>
<tr>
<th>Sample</th>
<th>ISO 25</th>
<th>ISO 40</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.76</td>
<td>6.95</td>
</tr>
<tr>
<td>2</td>
<td>2.59</td>
<td>2.00</td>
</tr>
<tr>
<td>3</td>
<td>0.60</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Yared & Bou Dagher 1994
Growth after extensive reaming: log10 values

Yared & Bou Dagher 1994
Growth after extensive reaming: Radio-assay

22 .. were instrumented with GT and Profile instruments to apical size #35 ..and 22 teeth with Pow-R instruments to apical size #50

Rollison S, Barnett F, Stevens RH. JOE 2002
Growth after extensive reaming: Radio-assay

Rollison S, Barnett F, Stevens RH. JOE 2002
Reduction in intracanal bacteria during root canal preparation with and without apical enlargement

Thirty-eight palatal roots of maxillary molar teeth were randomly assigned to two experimental and one control groups. The roots were reinfected with Enterococcus faecalis. All roots in the experimental groups were prepared in a step-down sequence with engine-driven GT rotary files at 350 rpm. In experimental group A (n = 16) additional apical enlargement to ISO size 35 was performed. In group B (n = 16) a serial step-back technique was followed with no apical enlargement. This was combined in groups A and B with irrigation with NaOCl and EDTA. In the control group (group C, n = 6) irrigation only was carried out, with no mechanical preparation. Samples were then taken from the root canals to determine the numbers of remaining bacteria.

Coldero LG, McHugh S, MacKenzie D, Saunders WP.

Int Endod J. 2002 May;35(5):437-46
Reduction in intracanal bacteria during root canal preparation with and without apical enlargement

Bacterial reduction with nickel-titanium rotary instrumentation.

Dalton BC, Orstavik D, Phillips C, Pettiette M, Trope M.

Department of Orthodontics, University of North Carolina School of Dentistry, Chapel Hill 27599, USA.
Study Design

- Human teeth, infected canals, *in vivo*
- Instrumentation with either Ni-Ti .04 taper rotary or stainless steel by hand
- Bacterial samples collected at increasing widths of instrumentation

Dalton et al. 1998
Growth after instrumentation: log10 values

<table>
<thead>
<tr>
<th>Sample</th>
<th>NiTi rotary</th>
<th>SS K-file</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>5.06</td>
<td>5.12</td>
</tr>
<tr>
<td>S2</td>
<td>3.32</td>
<td>3.13</td>
</tr>
<tr>
<td>S3</td>
<td>2.85</td>
<td>3.01</td>
</tr>
<tr>
<td>S4</td>
<td>2.44</td>
<td>2.68</td>
</tr>
</tbody>
</table>
Growth after extensive reaming: log10 values

Dalton et al., 1998
Radiographic Evaluation and Follow-Up

- Different methods of radiographic follow-up methods
- Assessment of one’s own cases
- Testing of medicaments, materials and techniques
Overview

• What is clinical research?
• Relevance: Legal aspects, manufacturers’ claims
• Importance: Necessary for improvement
• The relative irrelevance of experience
• Use of microbial markers
• The need for scepticism along side with enthusiasm
In the distant memory of the vital, uninflamed pulp: thank you for your attention!
Overview

• What is clinical research?
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Overview

• What is clinical research?
• Relevance: Legal aspects, manufacturers’ claims
• Importance: Necessary for improvement
• The relative irrelevance of experience
The 'boldness' of the radiographic contrast may lead us to assume better results than is actually the case.
35 asymptomatisk pulpitt

One visit endodontisk behandling med Epiphany/Resilon
46 Necrotic pulp

One visit endodontisk behandling med Epiphany/Resilon

Courtesy Dr Harald Prestegaard
47 partially necrotic pulp

One visit endodontisk behandling med Epiphany/Resilon

Courtesy Dr Harald Prestegaard
34 nekrotisk tann 2 kanaler

35 nekrotisk tann

Two visit endodontisk behandling med CaOH₂ og Epiphany/Resilon
Giant cell granuloma

2001 05 18 pain & infection
Clinical research: a definition with hows and whys

• Clinical studies: done at chairside
• Ex vivo
• In vivo
• In vitro
• Technological
Start PAI 4
Periapical changes after treatment

% healthy, PAI=1-2

Time, WEEKS

PAI 1
PAI 2
PAI 3
PAI 4
PAI 5
The case report: See what I can do, by listening, you share the glory
Best average

Typically institutional or specialist practice follow-up studies; the self-assured clinician comfortably states, "I have more than a 90 per cent success rate!"
Real average?

Cross-sectional, epidemiological approaches: the whole range; nobody wants to be associated with this.