



# Designing clinical trials to study early/immediate loading of dental implants

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## Lunch & Learning – designing trials on implant loading

- Background & experience
- Usage and future plans
- Any planned clinical study?

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## Immediate/early loading is beneficial? (SR #1—20, 2000- 2006)

1. 2006	Jokstad & Carr (lim. RCT+OCTs (22 of 187))
2.	Glauser ea. (17 of 240)
3.	Nkenke & Fenner (38)
4.	Del Fabbro ea. (71)
5. 2005	Ioannidou & Doufexi (13)
6.	Cooper ea (Edent. Maxilla (9)
7. 2004	Attard & Zarb (93)
8.	Esposito ea. (lim. Hi-quality RCTs (7))
9.	Misch ea. (24)
10.	Cochran ea & Morton ea & Chiapasco (Edent.(45) & Ganeles&Wismeijer (Single/PartialEdent. (25))
11.	Romanos (lim. Implant brand (10)
12.	Misch ea. (72)
13.	Castellon ea. (Mandible anterior (14))
14.	Esposito ea. (lim. Hi-quality RCTs (3))
15. 2003	Lekholm (15)
16.	Aparicio ea. (45)
17.	Gapski ea. (26)
18. <2003	Szmukler-Moncler ea. (2000)(16)

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**Immediate/early loading is beneficial? (SR #21—38, 2007-2010)**

2010  
 Ma & Payne (lim. Md 2IOD (25))  
 Alsabeeha ea. (lim. RCT+CCTs Md OD (10))  
 Atieh ea. (lim. SingleMolars+Postextraction( 9))

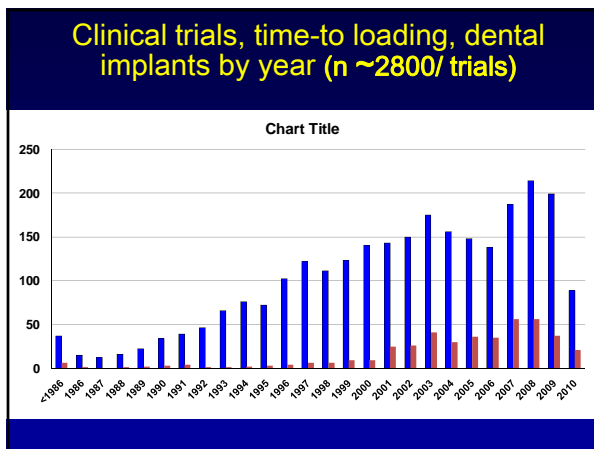
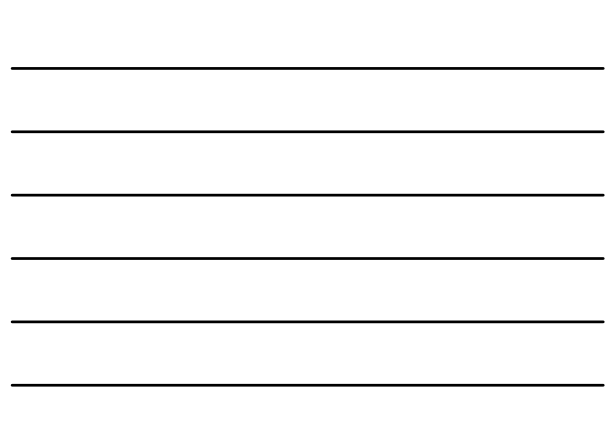
2009  
 Atieh ea. (lim. Single (5))  
 Atieh ea. (lim. Single+Postextraction (10))  
 Esposito ea. (lim. Hi-quality RCTs(22 of 30))  
 Gallucci ea. (lim. Edentulous; rough-surface-implants (61))  
 Rocuzzo ea. (lim. PartialEdent.PosteriorMax. (8 of 21))  
 Cordaro ea. (lim. PartialEdent.PosteriorMand. (19 of 28))  
 Grutter & Belsler (lim. PartialEdent.Anterior (10 of 29))

2008  
 DeRouck ea. (lim. Singleanterior+Postextr. (11))  
 Henry & Liddellow (lim. Best 20)  
 Sennnerby & Gottlow (lim. Publications>2005 (6))  
 Den Hartog ea. (lim. PartialEdent.Anterior 19 of 86)

2007  
 Esposito ea. (lim. Hi-quality RCTs(11 of 20))  
 Kawai & Taylor (lim. Md OD (9))  
 Avila ea. (28)  
 Jokstad & Carr (lim. RCT+CCTs (22 of 187))



Study	Esposito et al. (2007)	Jokstad & Carr (2007)	DeFabbro et al. (2006)	Nkenke & Feiner (2006)	Attard & Zarb (2005)	Cochrane et al. 111 Workshop (2004)
Dhanrajani & Al-Rafee 2005	---	Retro	---	---	---	---
Vanden Bogarde et al. 2005	---	CCT	---	---	---	---
Ostman et al. 2005	excluded	---	---	X	---	---
Nedir et al. 2004	---	CCT	---	---	---	---
Bischof et al. 2004	---	---	---	---	---	---
Saivi et al. 2004	excluded	---	---	---	---	X
Fischer & Stenberg 2004	X	RCT	---	---	X	X
Testori et al. 2004	---	excluded	X	X	X	---
Cannizzaro & Leone 2003	X	CCT	X	X	X	X
Ibanez et al. 2003	---	CCT	---	---	---	---
Malo et al. 2003	---	Retro	X	---	X	---
Testori et al. 2003b	excluded	CCT	---	---	X	---
Wolffinger et al. 2003	---	Submerg	X	---	X	X
Baishi & Wolffinger 1997	---	---	---	---	---	---
Depidi & Pistelli 2003	---	excluded	X	X	X	---
Rocci et al. 2003	---	excluded	X	X	X	---
Tawse-Smith et al. 2002	X	RCT	---	---	X	X
Payne et al. 2002	X	RCT	---	---	X	X
Romero et al. 2002	X	RCT	X	X	X	X
Gatti & Chiapasco 2002	---	excluded	X	X	X	---
Chansu et al. 2001	---	excluded	X	X	X	---
Chiapasco et al. 2001	X	RCT	X	X	X	X
De Bruyn et al. 2001	---	Submerg	---	---	X	---
Reynesdal et al. 2001	---	CCT	---	---	X	---
Ericsson et al. 2000	---	excluded	---	X	X	X
Rocuzzo et al. 2001	excluded	---	---	---	X	---
Jo et al. 2001	---	excluded	---	---	---	X
Random et al. 2001	---	excluded	---	---	---	X
Schuitman et al. 1997	---	Submerg	X	---	X	X
Schuitman et al. 1990	---	---	---	---	---	---
Tarnow et al. 1997	---	Submerg	X	---	X	---





## General findings RCT/CCT trials

### The first trials

- 1968 – 1975 (Brånemark et al. 1977: Experience from a 10-year period)
- TPS implants (Ledermann 1978); Tübinger Al<sub>2</sub>O<sub>3</sub> (Schulte 1978)

### The largest RCT trials

- 62 patients and 325 implants (Testori et al. 2008)
- 266 patients with 383 implants (Ganeles, Zollner, et al. 2008)

### The longest follow up RCT trial

- 5 years (Rocuzzo et al., 2008 & Fischer et al. 2008)

### The longest observation period

- 8-18 years, average 12, retrospective study on ITI implants placed in the edentulous mandible (Lambrecht & Hodel 2007)

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## Reason(s) for conducting a trial?

### ➤ PICOS question

- What is the relative merit / benefit ?
- What is the predictability ?

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	Relative merit of intervention	Predictability of intervention
1.	High quality RCT with narrow confidence Interval	Cohort study with ≥ 80% follow-up
2.	Cohort study or low quality RCT - e.g. <80% follow-up	Retrospective cohort study or follow-up of untreated control patients in an RCT
3.	Case-Control Study	
4.	Case-series (and poor quality cohort and case-control studies)	Case-series (and poor quality cohort studies)
5.	Expert opinion without explicit critical appraisal, or based on physiology, or bench research	Expert opinion without explicit critical appraisal, or based on physiology, or bench research

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## Reason(s) for conducting a trial?

### ➤ PICOS question

- What is the relative merit / benefit ?
- What is the predictability ?

*P*atient

*I*ntervention

*C*omparative intervention

*O*utcome

*S*tudy design

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## Developing the Study protocol

### ➤ Introduction

### ➤ M&M

- Sample size
- REB
- Funding?
- Recruiting clinicians / participants
  - Where? How?

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## Clinical variables with potential influence on treatment outcomes



- Patient inclusion and exclusion criteria (e.g. host factors, smoking, parafunction, bone type, etc.)
- State of dentition and intra-oral implant site
- Number of implants to support a superstructure
- Nature of implant-supported superstructure
- Clinical procedures (e.g. stage of healing following extraction, site preparation, torque, etc.)
- Implant morphology (smooth, microrough, rough)
- Treatment outcome criteria
- Observation period

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### Patient inclusion and exclusion criteria

- General
- Attitude / habits
- Medical
- Local
  - Anatomy
  - Pathology, current or past
- Operational

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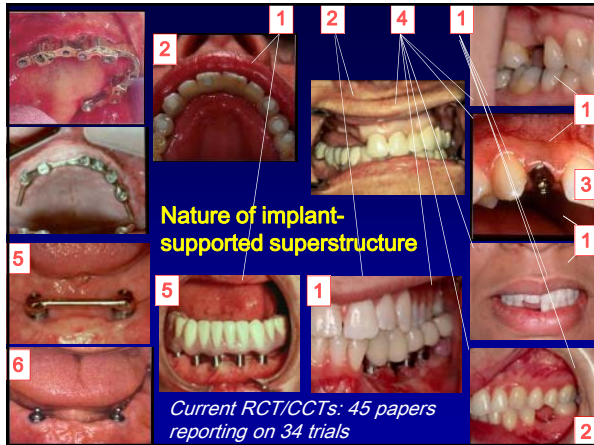
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### Clinical procedures (e.g. stage of healing following extraction, site preparation, torque, etc.)

Postextraction  
Instantly - hours -- 2 / 3 / 7 / 10 days- 2 weeks – 6-8 weeks – Healed 3 mths

Healing screw/cap -- Temporary / Permanent abutment / meso-structure?

Impression & Fixture – abutment / mesostructure?

Temporary, type and material – reline – occlusion ?

Final reconstruction – teeth in a day .... Teeth in an hour ....

No graft / graft / graft + membrane & Biomaterials(s)

Primary stability: 15 NCm --- 25 ---- > 50 NCm ? / .... 60 ? 70 ISQ

Primary stability not achieved – plan?

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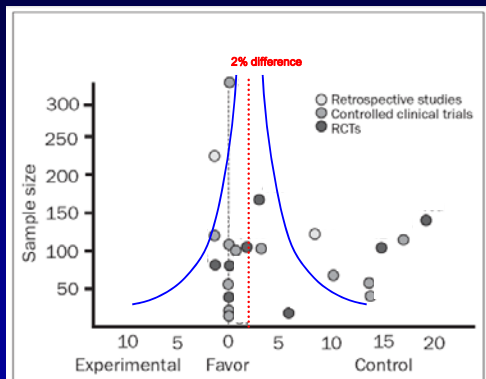
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## Implant morphology (smooth, microrough, rough)




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## Treatment outcome criteria

- Surrogates (?)
  - > 3D-fit of suprastructure / abutment
  - > 3D-position of implant
  - > Anatomy /-occlusion /-TMJ
  - > Biomarkers
  - > Bone /loss-gain on adjacent\_tooth /Gain /volume
  - > Detorque forces
  - > Histology
  - > Microbiota
  - > Operator assessed Esthetic / Function / Speech
  - > Papilla / Soft tissue / Volume
  - > Perioidices
  - > Implant Stability /Periost /\_RFA
- Patient Centered
  - > Adverse events: /-Altered Sensation /-apical /-Infraposition /-Pain /-Peri-implantitis
  - > Complications /-Biological / Technical
  - > Patient Diet / Esthetic // Function / QOL / Satisfaction / TMD
  - > Study Participation
  - > Success & Survival according to specific set of criteria e.g. Albrektsson et al. 1986
  - > Surgery success
- Societal
  - > Cost /time Maintenance /-of Prosthesis

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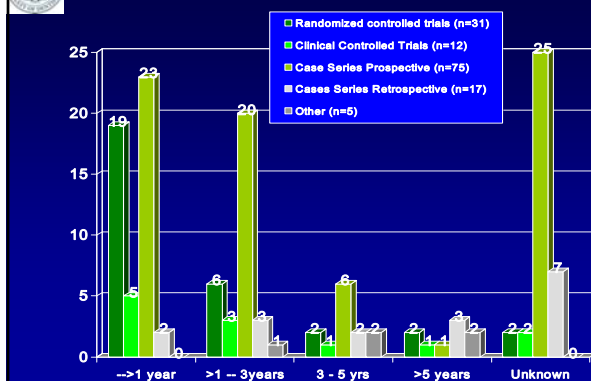
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## Observation Period




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