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?

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

Jokstad & Carr (lim. RCT+CCTs (22 of 187))
1. 2006   Glauser ea. (17 of 240)
2.   Nkenke & Fenner (38)
3.   Del Fabbro ea. (71)
4.   Ioannidou & Doufexi (13)
5. 2005   Cooper ea (Edent. Maxilla (9)
6.   Attard & Zarb (93)
7. 2004   Esposito ea. (lim. Hi-quality RCTs (7))
8.   Misch ea. (24)
9.   Cochran ea & Morton ea &
10.   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)

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

Year	Studies
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)
	Roccuzzo ea. (lim. PartialEdent.PosteriorMax. (8 of 21))
	Cordaro ea. (lim. PartialEdent.PosteriorMand. (19 of 28))
	Grutter & Belser (lim. PartialEdent.Anterior (10 of 29))
2008	DeRouck ea (lim. Singleanterior+Postextr. (11
	Henry & Liddelow (lim. Best 20)
	Sennerby & 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)	DelFabbro et al. (2006)	Nkenke & Fenner (2006)	Attard & Zarb (2005)	Cochrane et al. ITI Workshop (2004)
Dhanrajani & Al-Rafee 2005	---	Retro	---	---	---	---
Vanden Bogaerde et al. 2005	---	CCT	---	---	---	---
Ostman et al. 2005	---	excluded	---	X	---	---
Nedir et al. 2004 Bischof et al. 2004	---	CCT	---	---	---	---
Salvi et al. 2004	excluded	RCT	---	---	---	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	---	X	---
Wolfinger et al. 2003 Balshi & Wolfinger 1997	---	Submerg	X	---	X	X
Degidi & Piatelli 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
Romeo et al. 2002	X	RCT	X	X	X	X
Gatti & Chiapasco 2002	---	excluded	X	X	X	
Chausu et al. 2001	---	excluded	X	X	X	
Chiapasco et al. 2001	X	RCT	X	X	X	X
De Bruyn et al. 2001	---	Submerg	---	---	X	
Røynesdal et al. 2001	---	CCT	---	---	X	X
Ericsson et al. 2000	---	excluded	---	X	X	X
Roccuzzo et al. 2001	excluded	excluded	---	---	X	X
Jo et al. 2001	---	excluded	---	---	---	X
Randow et al. 2001	---	excluded	---	---	---	X
Schnitman et al. 1997 Schnitman et al. 1990	---	Submerg	X	---	X	X
Tarnow et al. 1997	---	Submerg	X	---	X	

Clinical trials, time-to loading, dental implants by year (n ~2800/ trials)

Chart Title

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_2O_3 (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 (Roccuzzo 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)

Reason(s) for conducting a trial?

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

	Relative merit of intervention	Predictability of intervention
1.	High quality RCT with narrow confidence Interval	Cohort study with $\geq$ 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

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

Developing the Study protocol

➢Introduction
➢M&M
  ➢Sample size
  ➢REB
  ➢Funding?
  ➢Recruiting clinicians / participants
    ➢Where? How?

## 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

Patient inclusion and exclusion criteria

➢ General
➢ Attitude / habits
➢ Medical
➢ Local
  ➢ Anatomy
  ➢ Pathology, current or past
➢ Operational
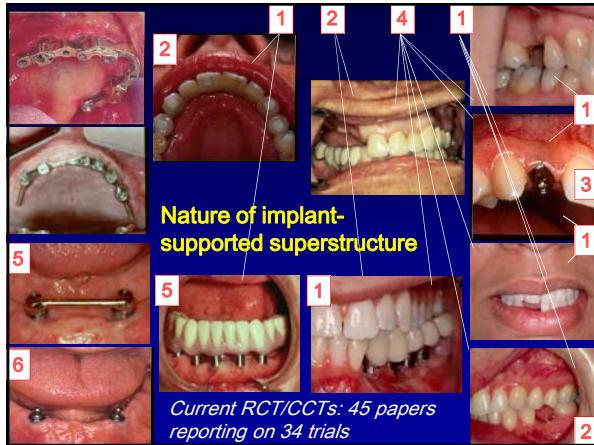
Nature of implant-supported superstructure

Current RCT/CCTs: 45 papers reporting on 34 trials

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

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

Implant morphology (smooth, microrough, rough)

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
- Perioindices
- Implant Stability   /Periotest /_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

Observation Period