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Early Loading Maxillary Cresco Full Arch Reconstructions. An RCT Trial.

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Background – Situation 2004

2000	**Re-focus on immediate loading of implants (Szmukler-Moncler et al. Clin Oral Impl Res 2000)**
2000-2004	**~350 clinical trials conducted on immediate and early loading**
	Distinct minority were RCTs. No studies with a primary focus on full jaw maxillary FDPs

Background – Situation 2004

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Authors	Patient Situation	Years	Implants	Prosthesis
Cannizzaro & Leone IJOMI 2003	Partial_dentate mandible&maxilla anterior&posterior	2	Spline Twist MTX	Crown+2-7i-FDP
Chiapasco / Gatti /Romeo et al. IJOMI 2001, COIR 2002	Edentulous mandible	2	Brånemark-Mk2 / Brånemark-Conical / ITI-sla	4i-Dolderbar-overdenture
Mau et al. IJOMI 2003	Edentulous mandible	5-1	IMZ / TPS	2i-bar- & 4i-bar-overdenture
Payne / Tawse-Smith et al., COIR 2001, 2002ab, 2003	Edentulous mandible	2	ITI-SLA / Southern / SteriOss / SteriOss-HL /	2i-ball-overdenture
Roccuzzo et al. COIR 2001	Partial_dentate mandible&maxilla posterior	1	ITI-sla & ITI-tps	"Crowns+FDPs"
Testori et al. PPAD 2003	Partial_dentate mandible&maxilla anterior&posterior	2-0.5	Osseotite & Osseotite NT	>2i-FDP

Background – Situation 2004

Assumptions:

1. A poor fit between a suprastructure and implants is associated with increased risk of technical and biological complications (Brunski , Adv Dent Res1999)

2. An improved fit will subject the supporting implants to less micromotion and thereby allow implant loading earlier than usual (Ericsson & Nilner , Int J Perio Restor Dent 2002)

Conventional casting without distortions is technique-sensitive

New fabrication techniques and position transfer devices have been developed to optimize FDP fit, e.g. , single-block milling and laser-welding

- **Cresco concept (Helldén et al. J Prosth Dent 1999; Int J Prosth 2003).**

Study designed in 2004/2005

Objective to appraise feasibility of interchanging conventional FDP with Cresco components in two different early loading protocols

Hypothesis 1: We expect no difference in bone loss between implants in the two Cresco-component FDPs versus implants supporting the conventionally made FDPs

Hypothesis 2: We expect no difference in bone loss between implants in the two Cresco groups when using a 10 days versus a 6-8 weeks post-healing loading protocol

Materials & methods

Materials & methods – Protocol development & administration

- **European Community Directive 2001/20 for Medical Devices introduced May 2004**
- **Regional ethics institutional board in Norway (#S-04162, P.I. Dr. Asbjorn Jokstad, Oslo) & Sweden (#M102-04, P.I, Dr. Stefan Ellner, Kalmar)**
- **Patient confidentiality procedures followed national regulatory standards. Norwegian Patient privacy ombudsman approval (#11123)**
- **ClinicalTrials.gov identification number: NCT00922935**
- **Randomization allocation was done by external third part (Analytica International, Lörrach, Germany)**
- **Study progress & Case Report Form (CRF) documentation monitored by study sponsor according to ISO 14155 guidelines for clinical investigations of medical devices**

Materials & methods: - Sample size calculation

- **Calculated for a two-sided test to compare two independent groups**
- **Standard deviation of bone levels in previously published clinical trials varies from 0.1 to 0.3mm (Esposito et al., Cochrane 2004)**
- **Anticipating a standard deviation of 0.2mm and considering a mean difference of 0.1mm bone loss between groups 1 and 2 and the control group at 1 year as clinically significant, a study with 80% power with an overall significance level of P=0.05 indicated a minimum of 22 patients per group.**

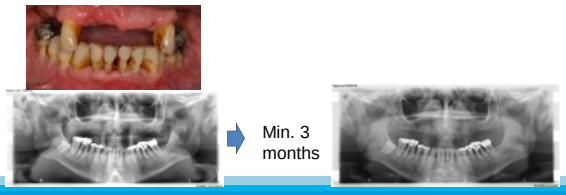
Materials & methods: - Study population

University clinic (Norway) + 4 public dental health centers (Sweden)

Patients with an edentulous maxilla desiring a 10/12-unit FDP

Recruited to partake in a blinded 3-arm RCT

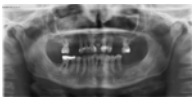
Fully healed maxilla with grafting ≥ 6 months previously



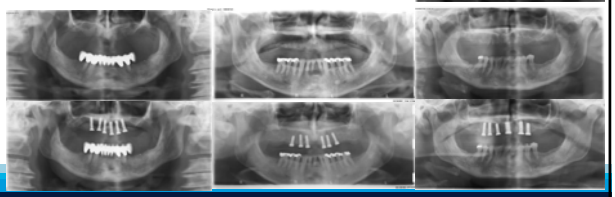
Inclusion criteria	Exclusion criteria
Aged ≥ 18 years	Systemic
Edentulous maxilla (at least 3 months before date of surgery) and request for implant-supported screw-retained FDP	Conditions requiring prolonged steroid use
GBR/GTR completed ≥ 6 months before implant surgery	History of leukocyte dysfunction or deficiency, bleeding disorders, neoplastic disease, renal failure, uncontrolled endocrine disorders
Adequate bone quality and quantity for placement of 3.3/4.1 mm implants without bone augmentation	Metabolic bone disorders
Agreement to participate in study up to 3 years follow-up	Physical handicaps that may affect oral hygiene maintenance.
	Use of investigational drugs ≤ 30 days before implant surgery
	Alcoholism or drug abuse
	HIV infection
	> 10 cigarettes or cigar or chew tobacco equivalents per day.
	Any conditions that may prevent study participation or interfere with analysis of results in the investigator's opinion
	Local
	Inflammation, including untreated periodontitis
	Mucosal diseases
	History of irradiation therapy
	Osseous lesions
	Unhealed extraction sites
	Bone surgery
	Severe bruxism/clenching
	Persistent intraoral infection
	Inadequate oral hygiene

Materials & methods: Surgical protocol

- Sterile conditions, local anesthetic and antibiotic coverage
- Standard implant placement protocol according to the manufacturer
- Six solid screw two-part implants ø3.3 or 4.1 mm (SLA Standard Plus, Straumann, Basel, Switzerland)



- Standard implant placement protocol according to the manufacturer
- Primary initial stability hand-tested by tightening of healing screw
- Symmetrical spread between tooth #4 and #13 (15-25)



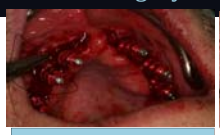
Materials & methods: Study Arms Allocation

•A sealed, numbered, opaque envelope containing the randomized allocation was sent to the clinician prior to each individual scheduled implant surgery

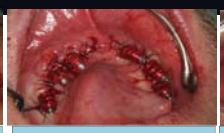
•Envelope opened first **after completion of the implant surgery**

•Randomization list generated by the external clinical research organization (CRO)
•Randomization list kept with the CRO for future reference and comparison with clinicians' lists
•Opened envelopes were kept as source documents for audit by the external CRO according to EC directives

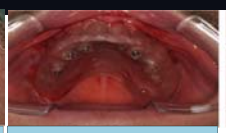
Materials & methods: Surgery session –impression/restoration protocol if immediate loading allocation



Impression copings & suturing



Ready for impression



Surgical stent used as impression tray

Hardened polyether impression elastomer

Maxillo-mandibular index, Hor. & Vertical

Impression pins removal, intaglio surf.

Healing caps placed

Old prosthesis relined with GC-Reline

Adopted from: Colomina Implant Dent 2001; Becker et al. J Periodontol 2003

Materials & methods: Study Arms & Interventions

Test group 1
FDP*, Cresco components (Cresco Ti Systems, Sarl, Lausanne, Switzerland)
Implants loaded within 10 d. post-implant placement

Test group 2
FDP*, Cresco components
Implants loaded 6-8 weeks post-implant placement

Control group
FDP*, conventional components
Implants loaded 6-8 weeks post-implant placement

***10-12 units, screw retained. Each centre used local Cresco-accredited laboratories & consistent dental technician & process**

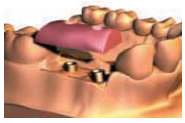
Materials & methods: Study Arms & Interventions

10-12 units, screw retained. Each centre used local Cresco-accredited laboratories & consistent dental technician & process

Photos:
Dr Stefan Ellner

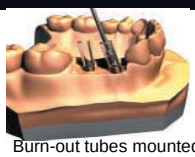
Cresco Ti system - Procedure used in 2004 for FDP fabrication

Cresco impression elements /pins in open/closed tray



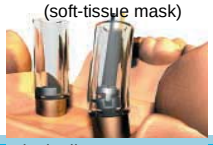
Cresco Replicas in stone master model (soft-tissue mask)

Mounted antagonist stone model in CR



Burn-out tubes mounted to replicas impression w/ process screw

Tubes bent (→17°) for optimal FDP design



Final adjustments & rotational placement

Final adjustments & vertical height cut

Wax-up of burn-out tubes

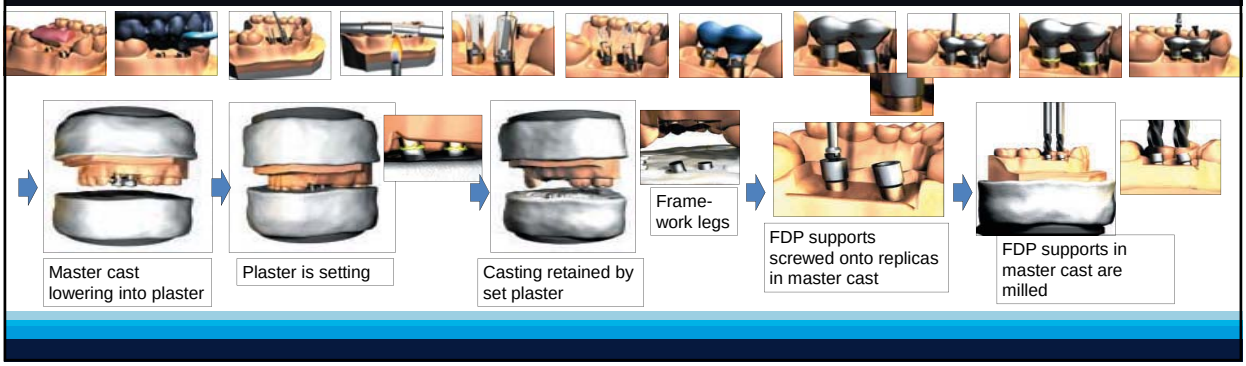
Cast framework

Potential casting distortion detection

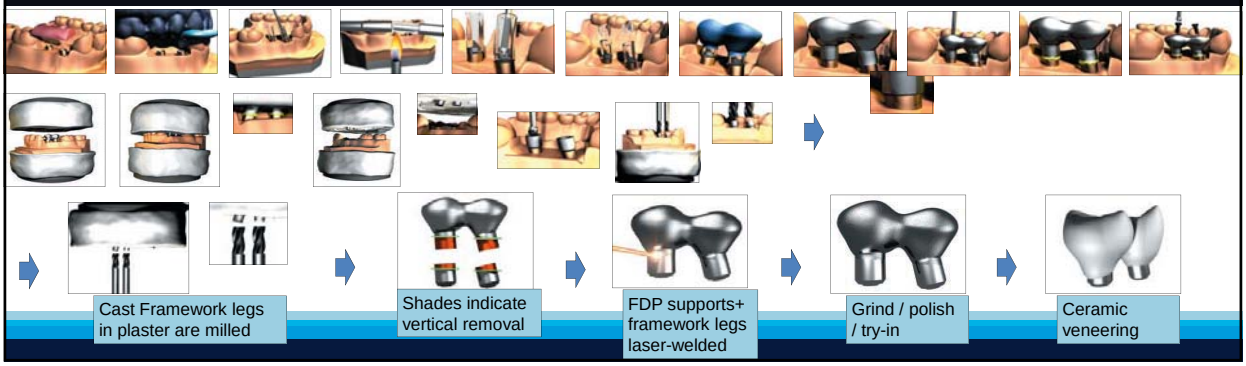
Cresco Ti system - Procedure used in 2004 for FDP fabrication

Relational transfer from stone cast to a “Cresco Fixator”

Cresco Ti system - Procedure used in 2004 for FDP fabrication



Cresco Ti system - Procedure used in 2004 for FDP fabrication



Materials & methods: Clinical outcomes

Patient complaints or any complications resulting from a change in health status

Any implant-related complications, e.g., pain, paraesthesia or peri-implant infection

Clinical-radiological examinations 3 & 6mths, 1, 2 & 3yrs

Periapical radiographs using customized film holders (Rinn XCP Film holder (Dentsply Rinn, Elgin, IL, USA) & a PVS putty impression)

Oral hygiene was assessed using sulcus bleeding, plaque index and oral hygiene criteria (Mombelli et al., Oral Microbiol Immunol 1987)

Patient satisfaction: perceived appearance, ability to chew, comfort, general satisfaction and ability to taste; rated: excellent / good / fair / poor

Materials & methods: Radiographic measurements

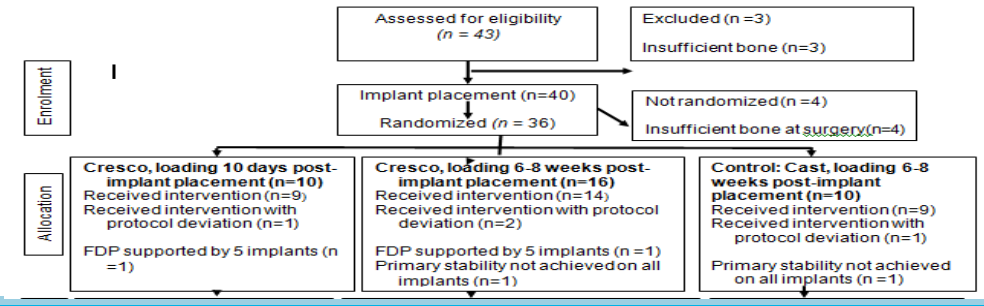
- **Same type of film used throughout the study for consistency.**
- **Radiographs digitized (Nikon Coolpix 995, Melville, NY, USA)**
- **Measurements using public domain software (ImageJ, NIH, Bethesda, USA)**
- **Bone level measurement performed independently by an investigator unrelated to the study**
- **Vertical distances in millimeters from the implant shoulder to the most apical initial point of first visible bone contact (depth of implant bone contact; DIB) measured for both proximal sites**
- **Eventual misalignments of the film planes relative to the implant long axis were accounted for by calibrating the software for each measurement to the known thread pitch of the implants (1.25 mm).**

Materials & methods: Statistical analyses

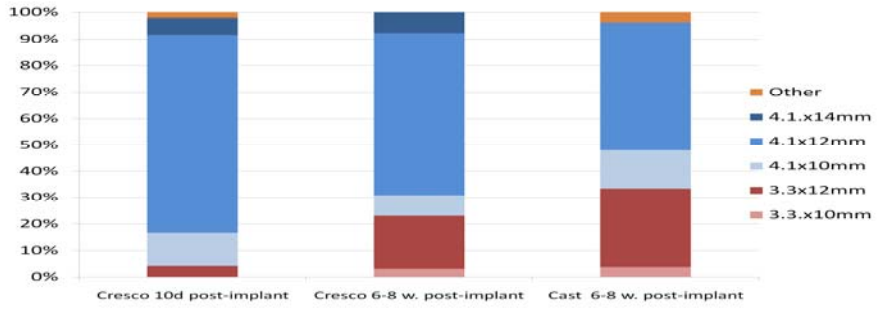
- **Two approaches: 1. All implants were taken into account, the patients build the clusters in the dataset. 2. Only one implant chosen as representative of all - both a mixed model and a cumulated logit model was applied**
- **The distribution of the continuous responses was appraised by the Kolmogorov-Smirnov test together with graphical presentation of the data**
- **K-S test indicated that the premises were adequate for using a "mixed model with random cluster-specific effect and fixed effects TIME, GROUP and TIME x GROUP"**
- **The dependent response in both types of analysis was the change of bone level over time; specifically the difference in bone level between the 3 groups, i.e. the response of a matched pair design, evaluated by paired t-tests.**
- **An ANOVA type model was used, especially a mixed model with random effect "patient" and fixed effects GROUP (3 levels), TIME, TIME x GROUP.**
- **All statistical analyses were done using SPSS statistical software (SPSS Inc., Chicago, IL, USA)**

Results

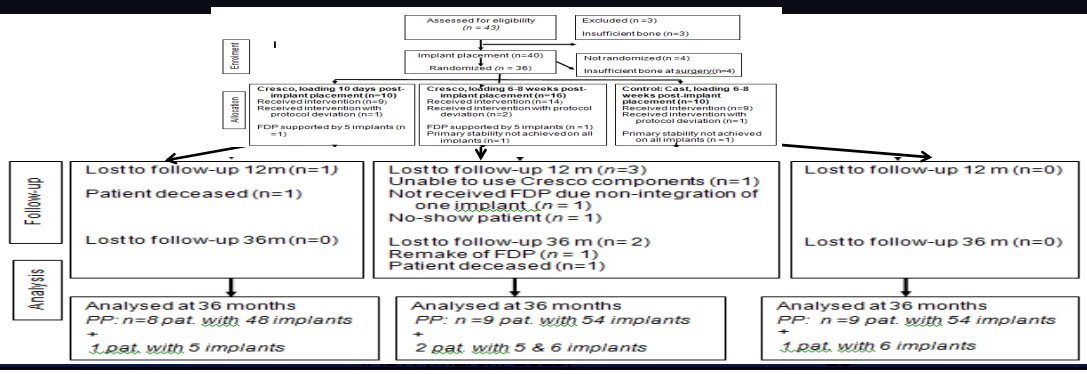
Results: Patient flow



Baseline data - Distribution of implant types



Results: Patient flow over 3 years



Results: Baseline (per protocol groups)

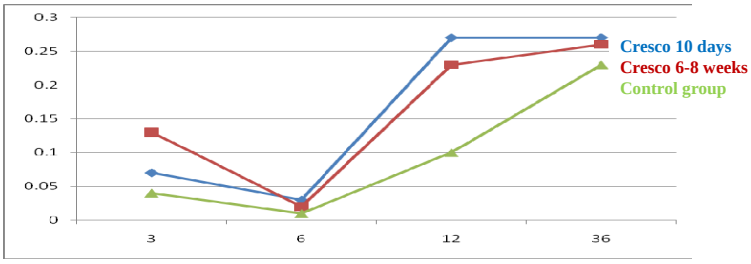
	Cresco 10d (n= 8 patients, 48 implants)	Cresco 6-8w (n= 9 patients, 54 implants)	Control 6-8w (n= 9 patients, 54 implants)	
Gender males (%)	5 (63)	6 (55)	1 (11)	*
Mean patient age (SD)	64 (12)	64 (11)	67 (7)	
Clinical team (1 - 5): patients (n)	1:3 2:1 4:3 5:1	1:3 2:1 3:2 4:3	1:3 2:3 4:2 5:1	
Bone quality (I - IV) (%)	II:37 III:50 IV:13	II:20 III:62 IV:18	II:0 III:56 IV:44	*
Bone form: knife (K) - parallel (P) - taper (T) - undercut (U) (%)	K:0 P:65 T:29 U:6	K:2 P:71 T:20 U:8	K:28 P:50 T:11 U:11	
Crest width: <5- 6-7-8 >8mm(%)	0 4 17 69 10 0	3 5 8 56 5 6	11 13 11 50 13 2	
Bone height: <10- 10/11-12/13 >13 mm (%)	15 15 54 17	2 12 73 23	13 17 69 2	
Implant depth (mm) (SD) (min - max) (distance cortical bone level to first implant thread)	2.9 (0.7) (1.3 - 4.2)	2.1 (0.6) (-0.3 - 3.3)	1.7 (0.9) (-0.6 - 1.9)	*

*Significant differences between the groups

Results – Clinical outcomes over 3 years

- **No implant-related complications**
- **A single occurrence of a localized peri-implantitis was treated uneventfully by penicillin.**
- **Prosthodontic complications and failures were rare (p> .05 amongst groups)**
- **Patient satisfaction scores were high in all 3 study groups regarding general satisfaction, comfort, satisfaction with appearance and ability to chew and taste (p> .05).**
- **Periodontal indices did not differ significantly amongst the three study groups (p> .05).**

Results: Average sulcus bleeding index over 3 years



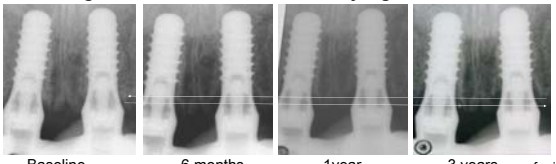
When a periodontal probe is passed along the gingival margin adjacent to the implant:
Score 0: no bleeding Score 1: isolated bleeding spot visible Score 2: blood forms a confluent red line on margin Score 3: heavy or profuse bleeding).

Results – Bone changes at the 3 years follow up

•The adjusted means and ranges of changes in crestal bone levels were:

- Group 1: -0.7 mm (-1.1 to -0.2)
- Group 2: -0.5 mm (-0.7 to -0.3)
- Group 3: -0.4 mm (-0.6 to -0.2) (p>0.05)

•The change from baseline was statistically significant in all treatment groups



Baseline 6 months 1year 3 years (#101 for illustration)

Results – Bone changes at the 3 years follow up

•The average bone loss was 0.5 mm for the medial pair, 0.9 mm for the two implants in the cuspid regions and 0.5 mm for the two most distal implants. Thus, the cantilever did not seem to accelerate bone loss on the most distally placed implants.

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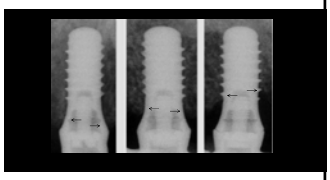
Conclusions

By assuming a non-inferiority margin of 0.3 mm bone loss:

1. Clinically relevant superiority of the Cresco groups vs the control group can be excluded

2. Inferiority of the Cresco groups compared to the control group cannot be excluded

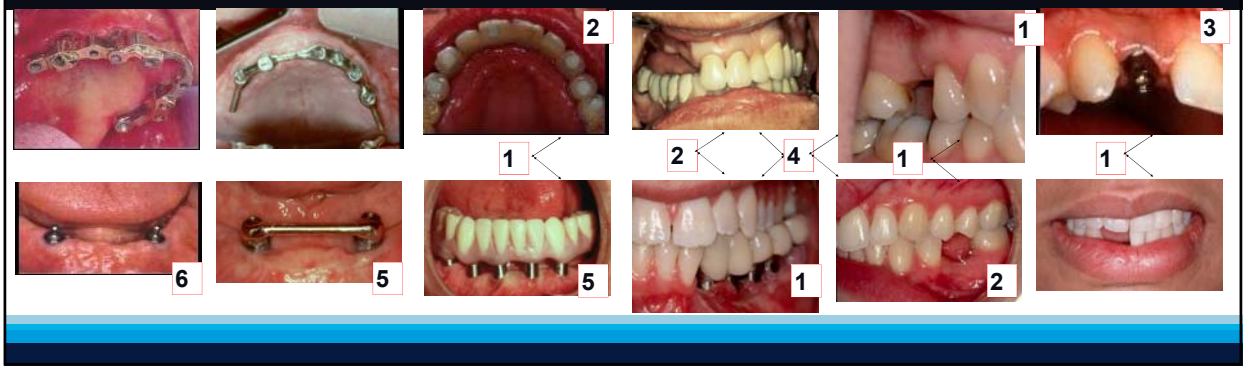


An additional change in bone level of -0.3 mm is expected by each 1 mm an implant is placed deeper

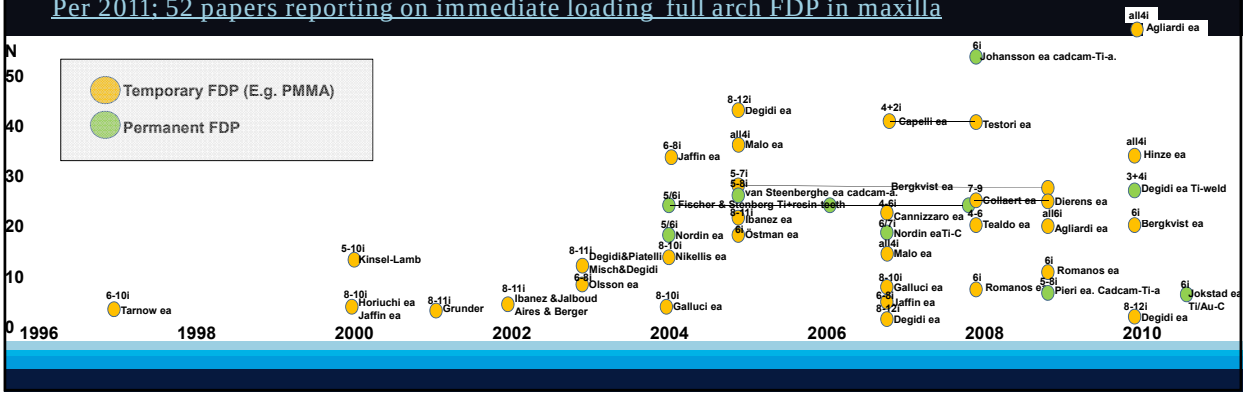
The vertical placement of the dental implant has more effect on bone loss than the fabrication technique used for the suprastructure and whether the implants were loaded after 10 days versus 6 to 8 weeks.

Discussion

Per 2011; 34 RCT /CCT trials comparing immediate vs delay loading - 3 w/ focus on full arch maxilla

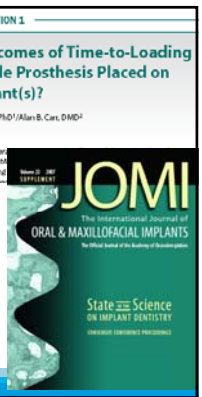


Per 2011; 52 papers reporting on immediate loading full arch FDP in maxilla



Confounding variables influencing the treatment outcome

- Patient inclusion and exclusion criteria (e.g. host factors, smoking, parafunction, bone type, etc.)
- State of remaining dentition and intra-oral implant placement site
- Number of implants to support the 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



Per 2011; 6 papers reporting Cresco-fabricated FDPs

Authors	Study type /Yrs	N pat.	Patient condition	Product (implants)	Cresco-Prosthesis	Survival (Imp.)(%)	Complications Biological/ technical
Helldén et al. Int J Pros 2003	Prospective 5 yrs	60	Edentul./ part. Dent. Md & Mx	Cresco-Ti (215)	"Fixed" (60)	98	Framework fracture (1) Screw fracture (6) Veneer fractures (5)
Hedkvist et al. Clin Imp Dent Rel Res 2004	Retrospective av.6 yrs	36	Edentul./ part. Dent. Md & Mx	Brånemark (207)	Ti+ acrylic-teeth (19)	99	Mucositis (13) Screwhole loss (4) Veneer fractures (3)
Hjalmarsson et al. Clin Imp Dent Rel Res 2005	Retrospective 3 yrs	23	Edentulous Mx	Astra (78)+ Brånemark (65)	Au/Ti+ acrylic-teeth (26)	98	Mucositis (5) Veneer fractures (4)
Nordin et al. Clin Oral Imp Res 2007	Prospective 2 yrs	19	Edentulous Mx	Straumann-SLA (116)	Ti+ acrylic-teeth (19)	98	Framework fracture (2) Rebase (2) Screw loose (2) Veneer fractures (7)
Hjalmarsson et al. Int J Pros 2011	Retrospective 5yrs	40	Edentulous Mx	Astra (213)+ (Brånemark / Straumann /3i (33))	Co-Cr+ceramic (15) Ti+acrylic-teeth (25)	99	Mucositis (5) Phonetics (2) Veneer fractures (4)
Jokstad et al. Clin Oral Imp Res 2011	**Prospective 3 yrs**	**17**	**Edentulous Mx**	**Straumann-SLA (102)**	**High noble + ceramic (17)**	**100**	**Unable to fabricate (1) Remake (1)**

Acknowledgments

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•Dagfinn Nilsen & Hans-Jacob Rønold (Oslo)
•Simon Dahlgren & Anders Teivik (Linkoping)
•Ulf Larsson (Kalmar)
•The statistical models were developed by Helge Toutenburg (†)
•Clinical research management by Dr Kristina Espemar Holst, Straumann

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