What is the clinical relevance of animal models for evaluating bone & cell responses *vz* implant design & roughness?

Asbjørn Jokstad
University of Toronto

What is the relevance of data from animal models to predict longitudinal trial results?

A: Very high

B: High

C: Uncertain value

D: Of little value

E: Of no value

The relevance of data from animal models to predict longitudinal trial results?

- is high?

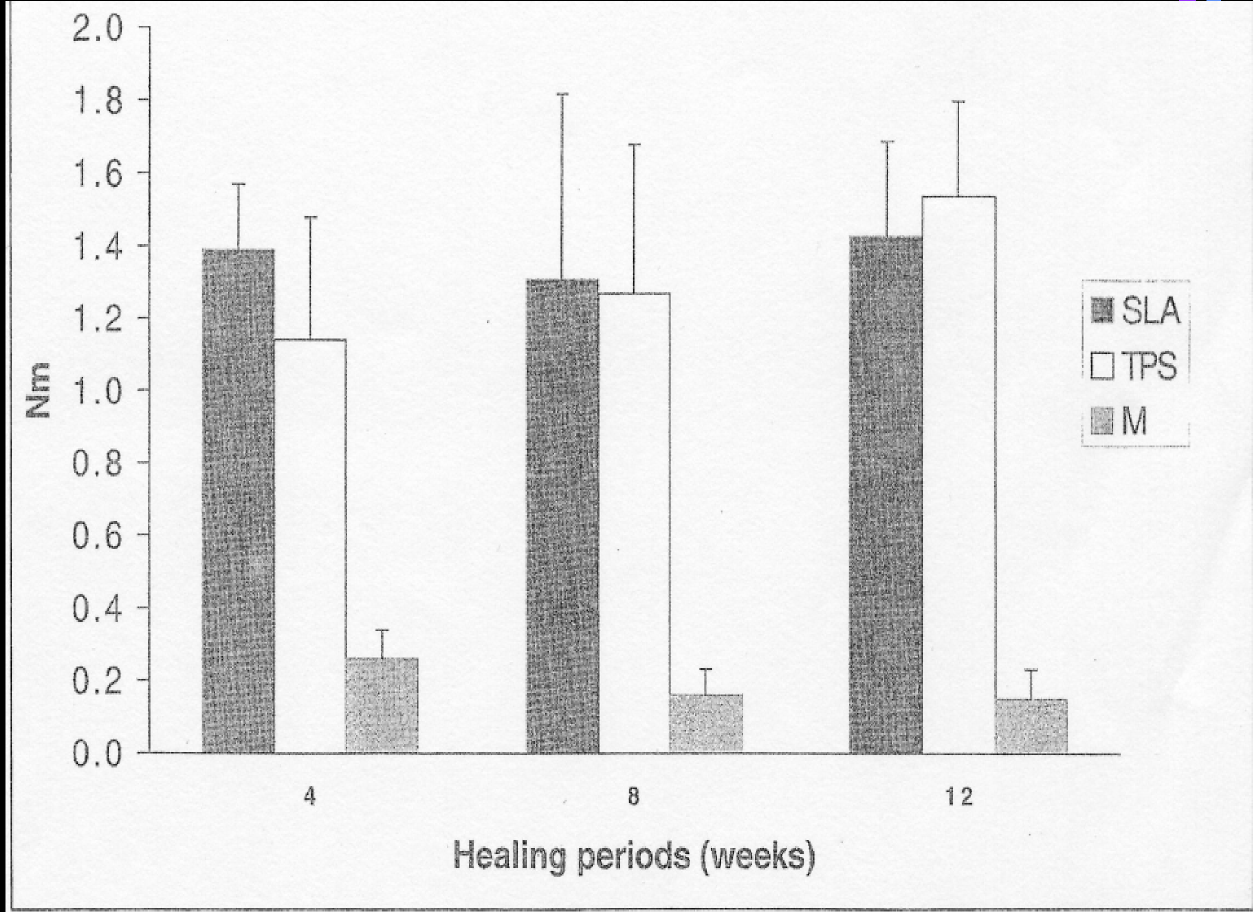
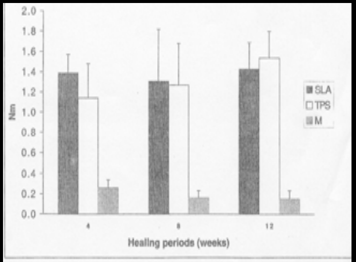


Figure 1. Removal torque values (RTV) in Newtonmeters (Nm) of three implant types machined (M), titanium-plasma-sprayed (TPS), and sandblasted with large-grit and acid-attacked (SLA) surfaces after 4, 8, and 12 wks of healing in the maxillae of miniature pigs (from Buser *et al.*, 1999b; reprinted with permission).

The relevance of data from animal models to predict longitudinal trial results?



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- is high?
- is of little or no value?
  - London et al. 2002; Novaes et al. 2002; Carlsson et al. 1988; Gotfredsen et al. 1992; Vercaigne et al. 1998, 2000.
- Offers some indications within a midrange of roughness?
  - Wennerberg & Albrektsson, 2000

Relevance animal models *vz.* longitudinal trial results?

- Surface topography description?

Table 1 Definition of Selected Standard ("Integral") 2-D Roughness Parameters with Respect to Amplitude, Spacing, or Combined Amplitude and Spacing Characteristics

Roughness parameters	Definition	Type*	Description
R_a (µm)	$R_a = \frac{1}{m}\sum_{i=1}^{m} \lvert z(x_i) \rvert$	A	The arithmetic average of the absolute values of all points of the profile; also called CLA (center line average height)
R_q (µm)	$R_q = \sqrt{\frac{1}{m}\sum_{i=1}^{m} z^2(x_i)}$	A	The root mean square (RMS) of the values of all points of the profile
R_t (µm)		A	The maximum peak-to-valley height of the entire measurement trace
R_{zDIN} (µm)	$R_{zDIN} = \frac{1}{5}\sum_{i=1}^{5} z(x_i)$	A	The arithmetic average of the maximum peak to valley height of the roughness values $z(x_1)$ to $z(x_5)$ of 5 consecutive sampling sections over the filtered profile
S_m (mm)	$S_m = \frac{1}{m}\sum_{i=1}^{m} S_i$	S	Arithmetic average spacing between the falling flanks of peaks on the mean line
S_k	$S_k = \frac{1}{n}\sum_{i=1}^{n} \frac{y_i^3}{R_q^3}$	H	Amplitude distribution skew $S_k = 0$: amplitude distribution is symmetric $S_k < 0$: profile with "plateaus" and single-deep valleys $S_k > 0$: profile with very intense peaks
L_r	$L_r = \frac{L_0}{L_m}$	H	The relationship of the stretched length of the profile L_0 to the scanned length L_m

*A – amplitude; S – spacing; H – hybrid parameter (combined amplitude and spacing).

Wieland et al. Int J Oral Maxillofac Implants 2001;16:163–181)

Relevance animal models *vz.* longitudinal trial results?

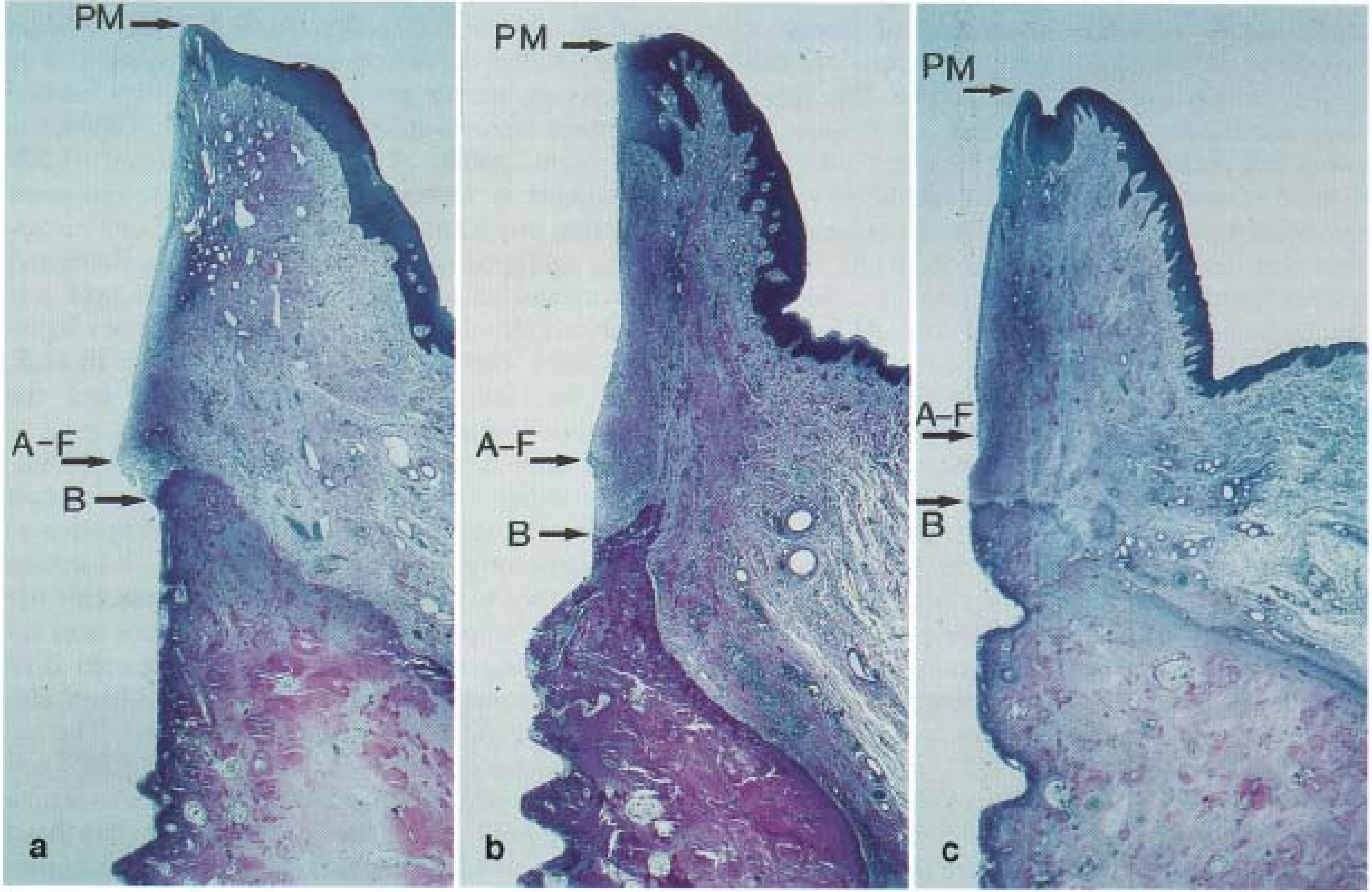
- Surface topography description?
- Model used?

Table 2 Biomechanical Studies of the Bone-Implant Interface

Model	Implant type	Observation time	Biomechanical result	Biomechanical test
Goat mandible and maxilla[151]	Cylindric 4 × 1 1-mm TPS	2 to 24 wk	50 to 1,000 N	Pull-out
Canine mandible[150]	Cylindric 3/3.3/4 × 4/8/15-mm HA	15 wk	130 to 282 MPa	Pull-out
Canine mandible[149]	Threaded/cylindric 4 × 10-mm HA	15 wk	4.61 to 6.85 MPa	Pull-out
Rat tibia[177]	Threaded 2 × 2-mm cpTi	8 wk	10 to 32 MPa	Pull-out
Rabbit femur[178]	Cylindric 2 × 12-mm cpTi, HA-glass	3, 6, and 9 wk	4.5 to 27 MPa	Pull-out
Canine femur[179]	Cylindric 4.7 × 12-mm Ti alloy, HA-coated	12 and 24 wk	14 to 16 MPa	Pull-out
Canine mandible[153]	Threaded 4 × 14-mm cpTi	0 and 3 mo	813 to 1,194 N	Push-out
Canine femur[154]	Cylindric 6 × 13-mm Ti alloy, HA	4 and 12 mo	0.1 to 11.7 MPa	Push-out
Canine femur[155]	Cylindric 4 × 15-mm carbon, HA, Ti alloy	8 wk	1.59 to 8.71 MPa	Push-out
Rabbit femur[157]	Cylindric 2.8 × 6-mm HA, Al_2O_3	3 mo	3 to 15 MPa	Push-out
Canine femur[156]	Cylindric 10 × 10-mm HA, glass-ceramic	12 wk	0.24 to 3.84 MPa	Push-out
Goat tibia[180]	Cylindric 4 × 10-mm Ti alloy, TPS	3 mo	2.9 to 12.9 MPa	Push-out
Canine humerus[181]	Cylindric 6 × 10-mm Ti alloy, HA, TPS	6 wk	0.31 to 3.4 MPa	Push-out
Rabbit tibia and femur[160]	Threaded 3.75 × 6-mm cpTi, blasted	12 wk	9 to 65 Ncm	Torque
Rabbit tibia and femur[159]	Threaded 3.75 × 4-mm cpTi	6 wk and 3 and 6 mo	20 to 37 Ncm	Torque
Rabbit tibia[161]	Threaded, cylindric 3.5 × 10-mm cpTi machined, blasted, HA	3 and 12 wk	20 to 117 Ncm	Torque
Rabbit femur[107]	Threaded 3.25 × 4 mm cpTi, machined, acid-etched	2 mo	1.8 to 36.1 Ncm	Torque
Miniature pig maxilla[109]	Threaded 3.75 × 10-mm, 4 × 8-mm TPS, acid-etched	4, 8, and 12 wk	46 to 227 Ncm	Torque
Rabbit femur and tibia[98]	Threaded 3.75 × 6-mm cpTi, machined, blasted	12 wk	10 to 60 Ncm	Torque
Canine mandible[182]	Threaded, cylindric 3.5 × 10-mm cpTi, machined, blasted	12 wk	22 to 150 Ncm	Torque
Baboon mandible and maxilla[183]	Threaded 3.8 × 10-mm cpTi, Ti alloy, HA	3 to 4 mo	65 to 168 Ncm	Torque
Rabbit tibia[40]	Threaded 3.75 × 6-mm cpTi, Ti alloy	3 mo	18 to 86 Ncm	Torque

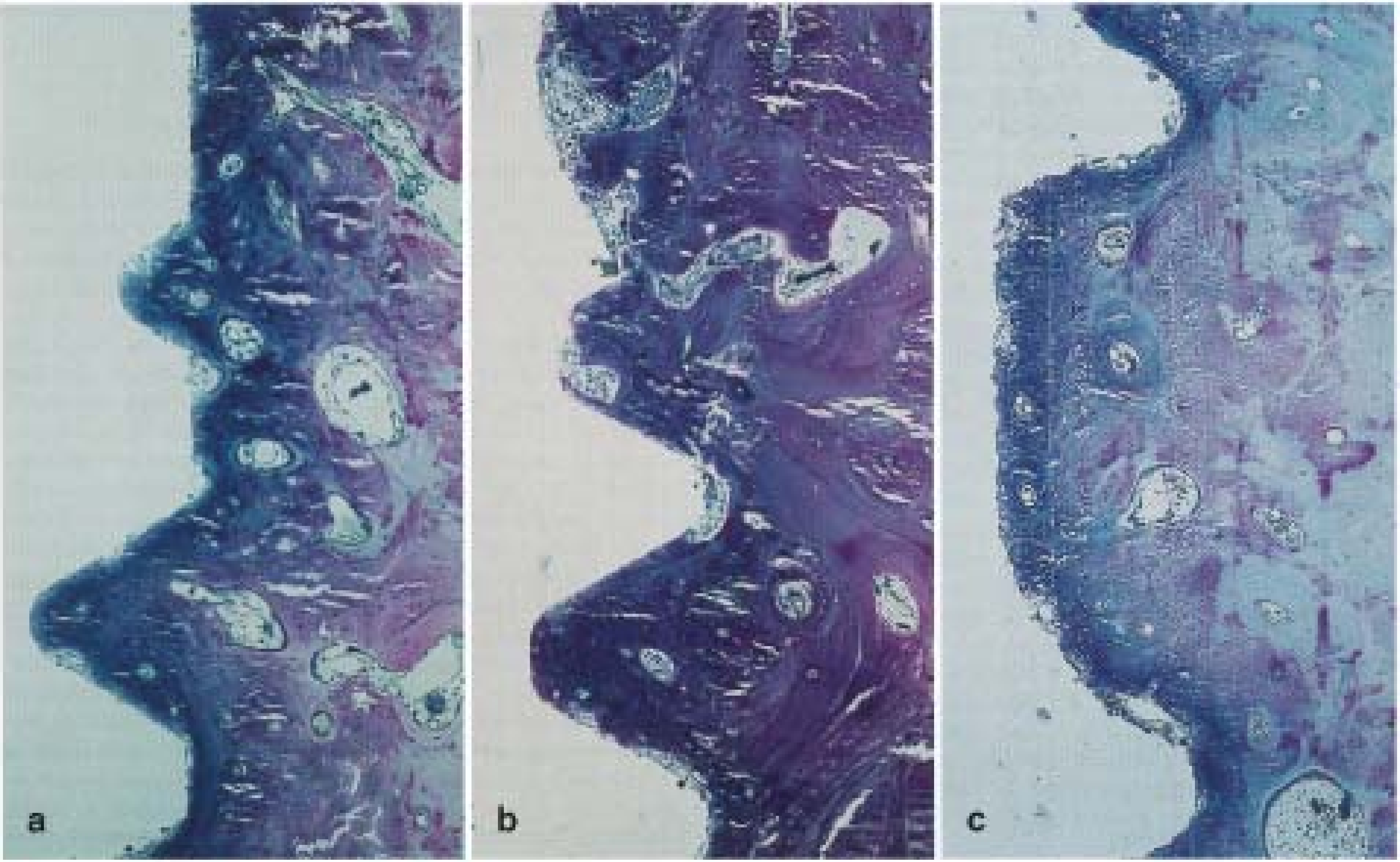
TPS = plasma-sprayed titanium; HA = hydroxyapatite; cpTi = commercially pure titanium; wk = weeks; mo = months.

Sykaras et al., 2000



Astra Branemark ITI

Abrahamson et al. 1996



Astra Branemark ITI

Abrahamson et al. 1996

Table 3 Histomorphometric Studies of the Bone-Implant Interface

Model	Implant type	Observation time	Bone-implant contact (%)
Canine mandible[167]	Threaded Ti	5 to 24 mo	50 to 65
	Threaded ceramic		41
Rabbit tibia[162]	Threaded Ti	4 wk	20 to 36
Sheep tibia[184]	Threaded cpTi	6 mo	56 to 60
Canine mandible[185]	Threaded cpTi	4 mo	42 to 70
Baboon mandible and maxilla[186]	Threaded cpTi, alloy	3 mo	40
	Threaded HA		62
Baboon mandible[187]	Cylindric HA	6 mo	67
Rabbit knee and tibia[159]	Threaded cpTi	6 wk, 3 mo, and 6 mo	21 to 58
Canine mandible[164]	Cylindric TPS	3 mo	48
Canine mandible[165]	Threaded Ti	3 mo	46
	Cylindric TPS		55
	Cylindric HA		71
Rhesus monkey mandible[169]	Porous	74 mo	64 to 67
Human biopsies[188]	Threaded cpTi	1 to 16 y	43 to 100
Canine mandible and maxilla[189]	Threaded cpTi	5 mo	46 to 60
Ewe femur[163]	Threaded cpTi	12 wk	61 to 68
Human biopsies[168]	Threaded cpTi	8 to 20 mo	34 to 93
Human biopsies[166]	Threaded hollow cpTi	23 to 36 mo	18 to 74
	Cylindric hollow cpTi		
Canine mandible[190]	Threaded hollow cpTi	3, 6, and 15 mo	52 to 78
Rabbit tibia[40]	Threaded cpTi, alloy	3 mo	21 to 46
Human biopsies[191]	Threaded cpTi	24 mo	61 to 69
Canine mandible[192]	Cylindric cpTi	12 wk	2 to 100
Human biopsies[193]	Threaded hollow cpTi	6 mo	17 to 72
Monkey mandible[194]	Threaded cpTi	18 mo	11 to 73

Ti = titanium; cpTi = commercially pure titanium; TPS = plasma-sprayed titanium; HA = hydroxyapatite; wk = weeks; mo = months; y = years.

Parameters affecting histologic/biomechanical data

Implant length	Implant diameter	Implant design	Implant material
Surface topography	Animal model	Implantation time	Implantation site
Biomechanical loading speed	Functional loading conditions	Analyzed length	Orientation of histologic section

Sykaras et al., 2000

Relevance animal models *vz.* longitudinal trial results?

- Surface topography description?
- Model used?
- Roughness characterization?

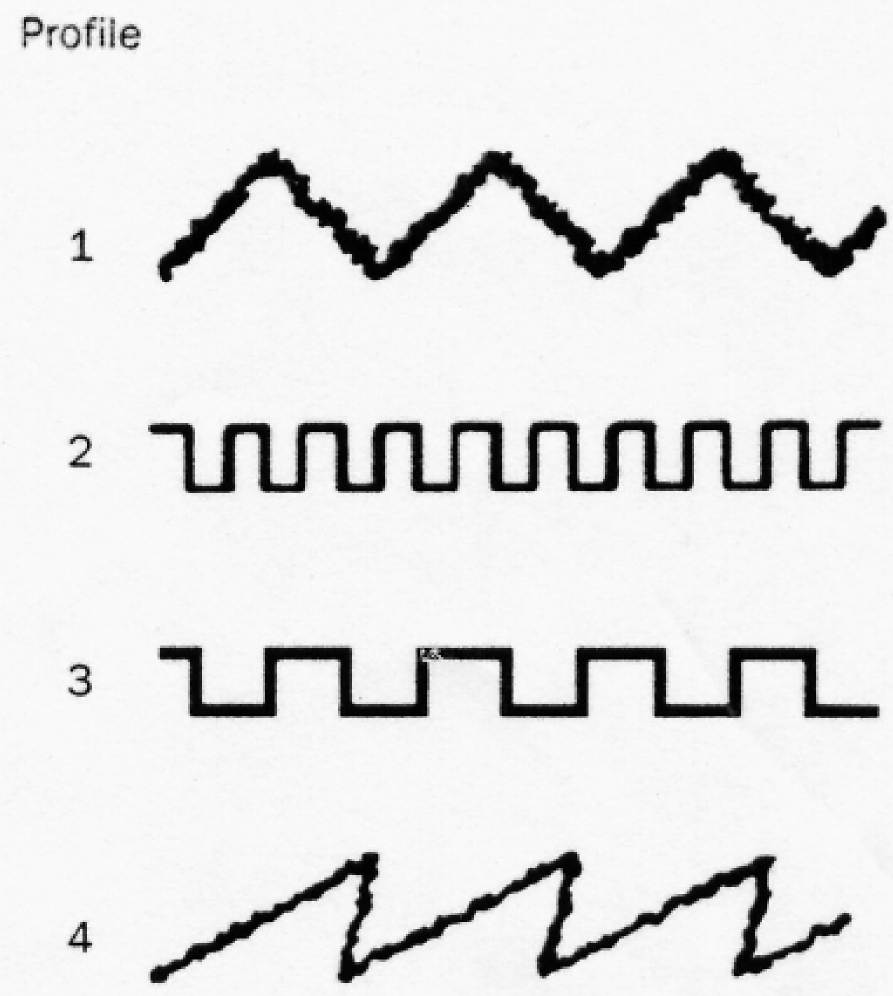


Fig 6 Four different profiles with the same average height deviation (R_a).

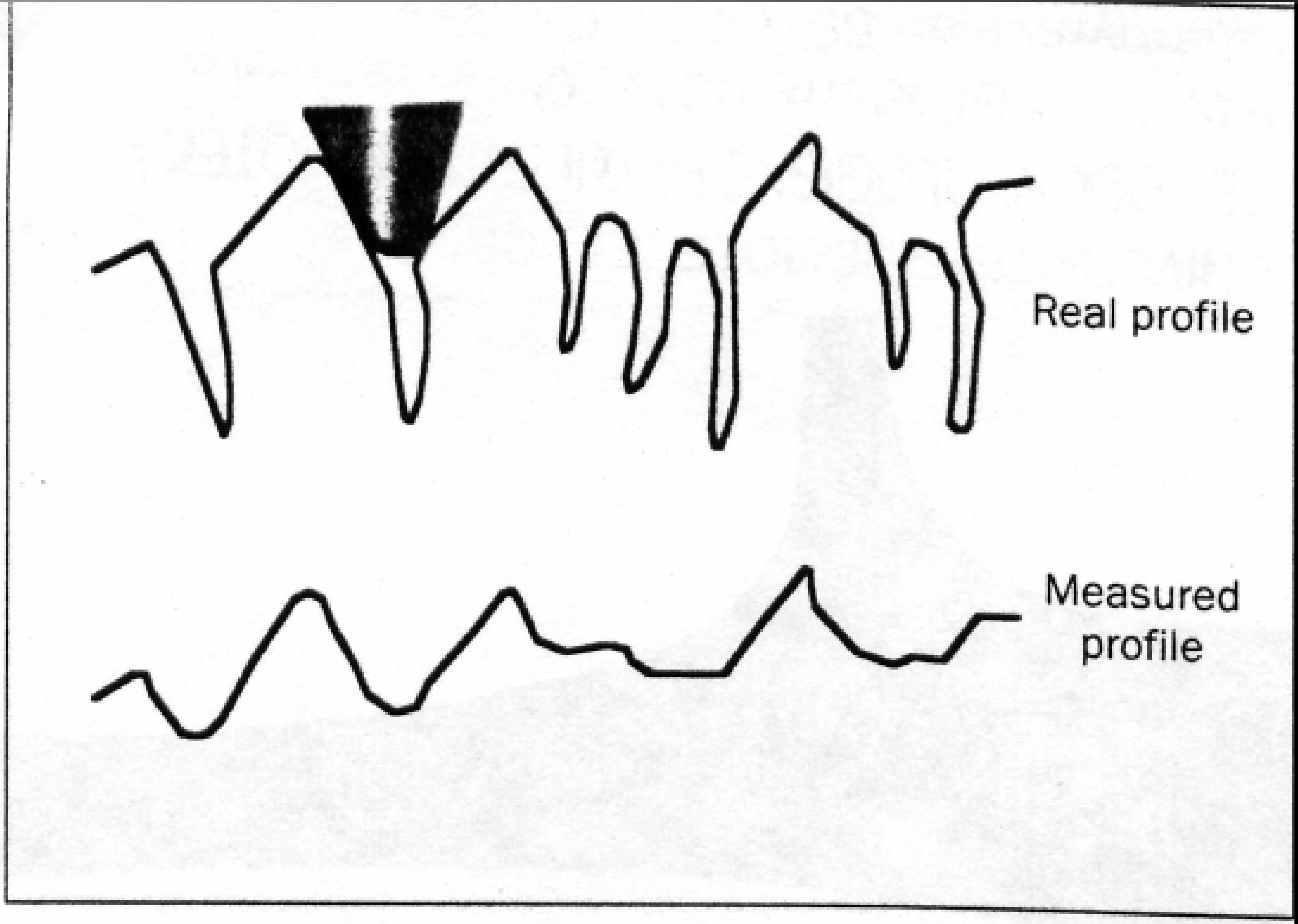


Fig 1 Diagram of the influence of tip radius on the measured profile. A radius that is too large will result in a loss of information.

Relevance animal models *vz.* longitudinal trial results?

- Surface topography description?
- Model used?
- Roughness characterization?
- Measuring device?

Table 2 Advantages and Limitations of the Techniques Used in this Study to Characterize Surface Topographies

Method (environment)	Advantages	Limitations
Non-contact laser profilometry (air)	Non-contact, non-destructive Fast for 2-D profiles (minutes) Resolution: vertical about 50 nm, lateral about 1 µm Scanning over mm to cm possible	Artifacts (optical effects at sharp edges, reflections at locally shiny areas) Time-consuming for 3-D images (h)
Interference microscopy (air)	Non-contact, non-destructive Fast (3-D images, minutes) Resolution: vertical about 1 nm, lateral about 0.2 µm	Only small area measured at high lateral resolution For larger areas, adjacent images with high resolution have to be combined
Scanning electron microscopy (high vacuum)	High resolution: vertical 1 nm, lateral 10 nm High depth of focus Morphologic information Local chemical analysis (electron dispersive spectroscopy)	No quantitative topographic information
Stereo-scanning electron microscopy (high vacuum)	High depth of focus High dynamic x,y,z-range (mm to nm) Resolution: vertical 0.5 µm to 0.1 µm, lateral 20 nm to 50 nm Quantitative topographic information (2-D)	Not widely used Unsuitable for smooth surfaces Only small area at high lateral resolution For larger areas, adjacent micrographs with high resolution have to be combined
Atomic force microscopy (air, liquid, vacuum)	Highest resolution in both lateral and vertical directions (atomic to nm)	Limited z-range (problems with rough surfaces) Artifacts (envelope effect because of tip shape, surface deformation), particularly for high-aspect-ratio surfaces

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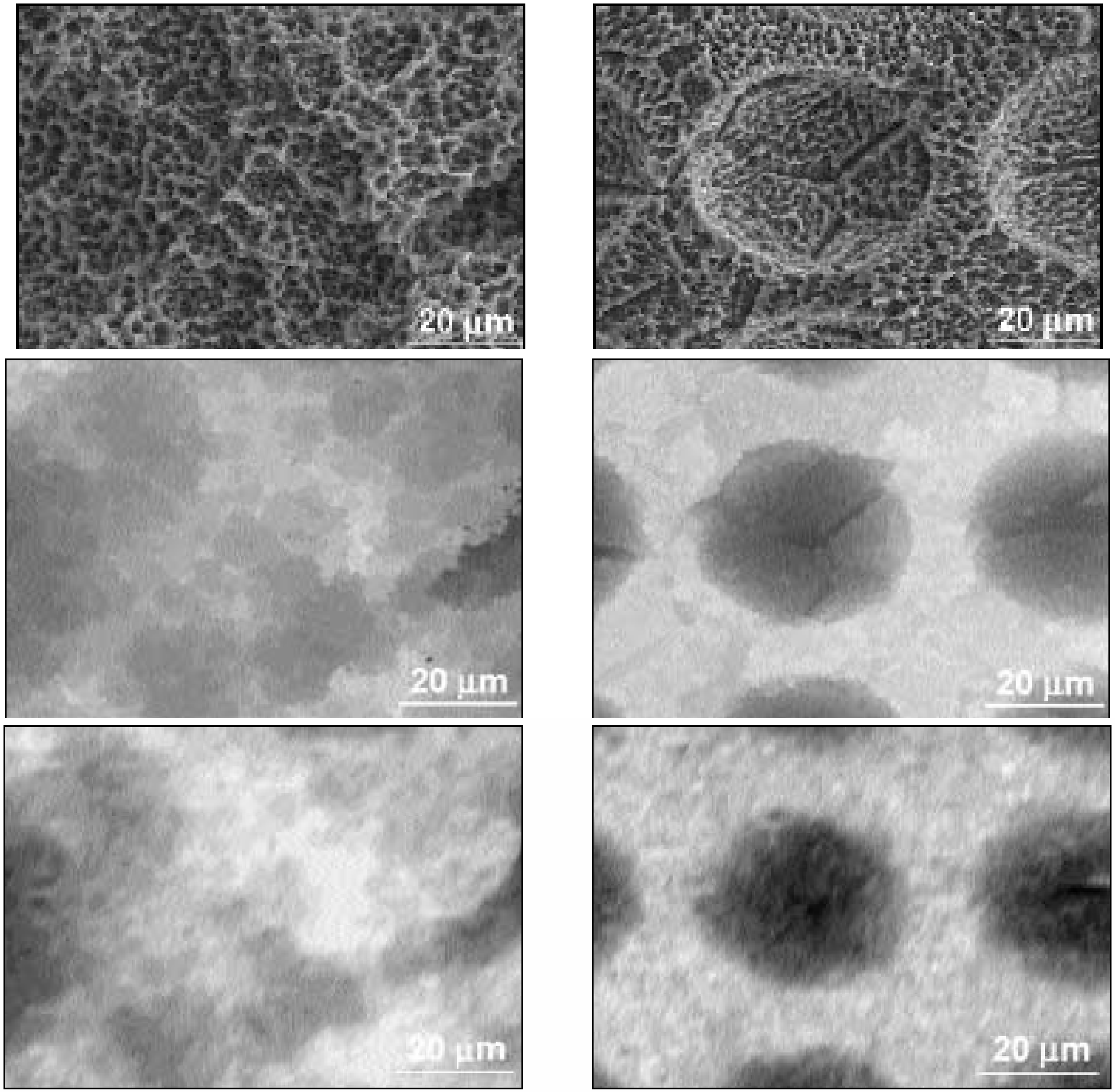
Grit-blasted and etched | Microfabricated and etched



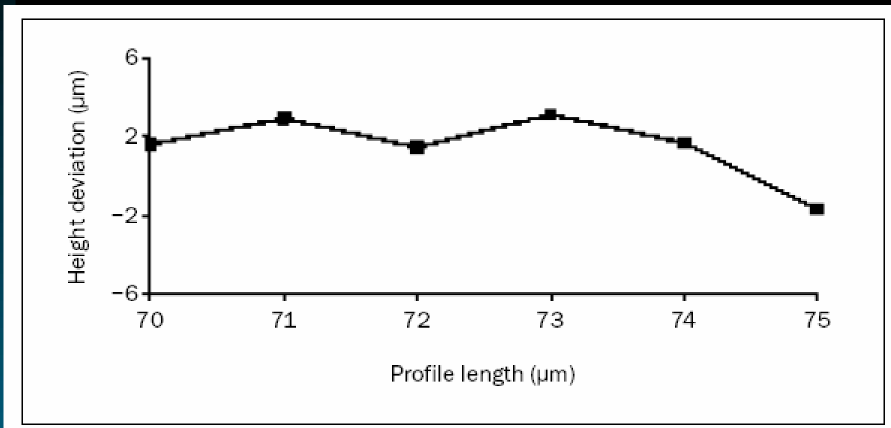
Scanning EM

Interference microscopy

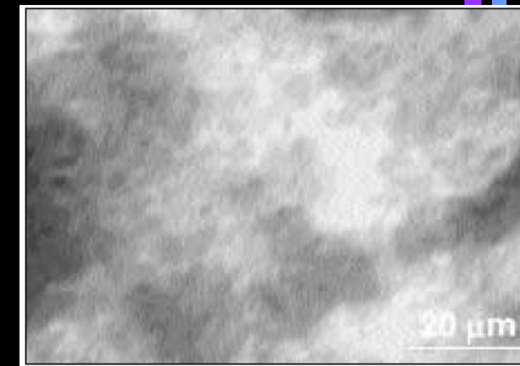
Non-contact laser profilometry

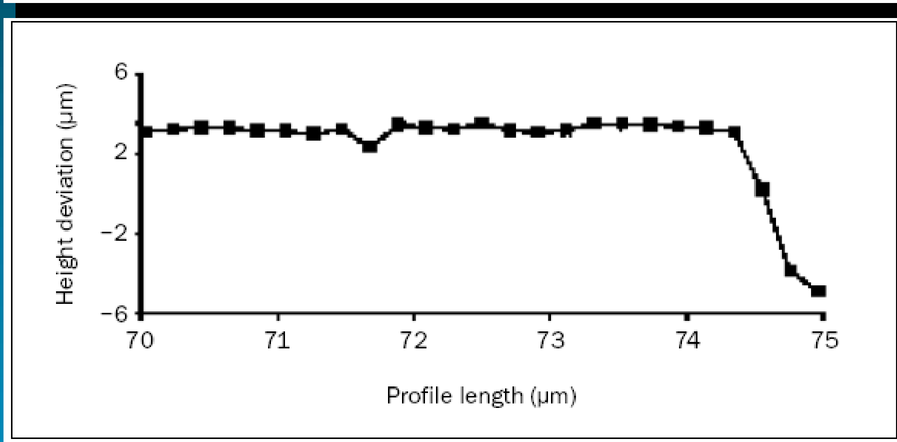
Wieland et al. 2001

Grit-blasted and etched

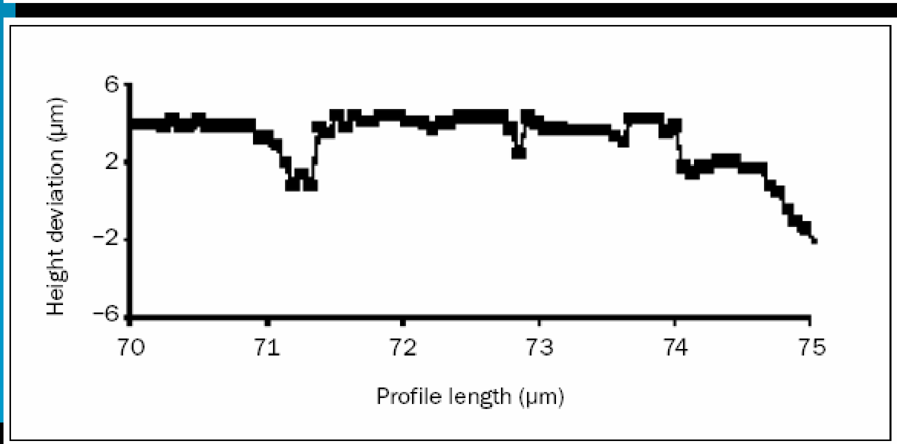


Laser profilometry

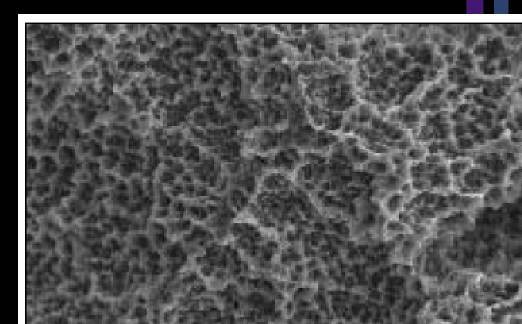




Interference microscopy



Scanning EM



Wieland et al. 2001

Relevance animal models *vz.* longitudinal trial results?

- Surface topography description?
- Model used?
- Roughness characterization
- Measuring device
- Consistency of results?

Implant Surface Roughness and Bone Healing: a Systematic Review
M M Shalabi; A Gortemaker; M A Van't Hof; J A Jansen; N H J Creugers
Journal of Dental Research; Jun 2006; 85, 6; Career and Technical Education
pg. 496

CRITICAL REVIEWS IN ORAL BIOLOGY & MEDICINE

Implant Surface Roughness and Bone Healing: a Systematic Review

M.M. Shalabi[1], A. Gortemaker[1], M.A. Van't Hof[2], J.A. Jansen[1]*, and N.H.J. Creugers[3]

[1]Department of Periodontology and Biomaterials, [2]Biostatistics, and [3]Department of Oral Function and Prosthetic Dentistry, Dentistry 309, College of Dental Science, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands; *corresponding author, j.jansen@dent.umcn.nl

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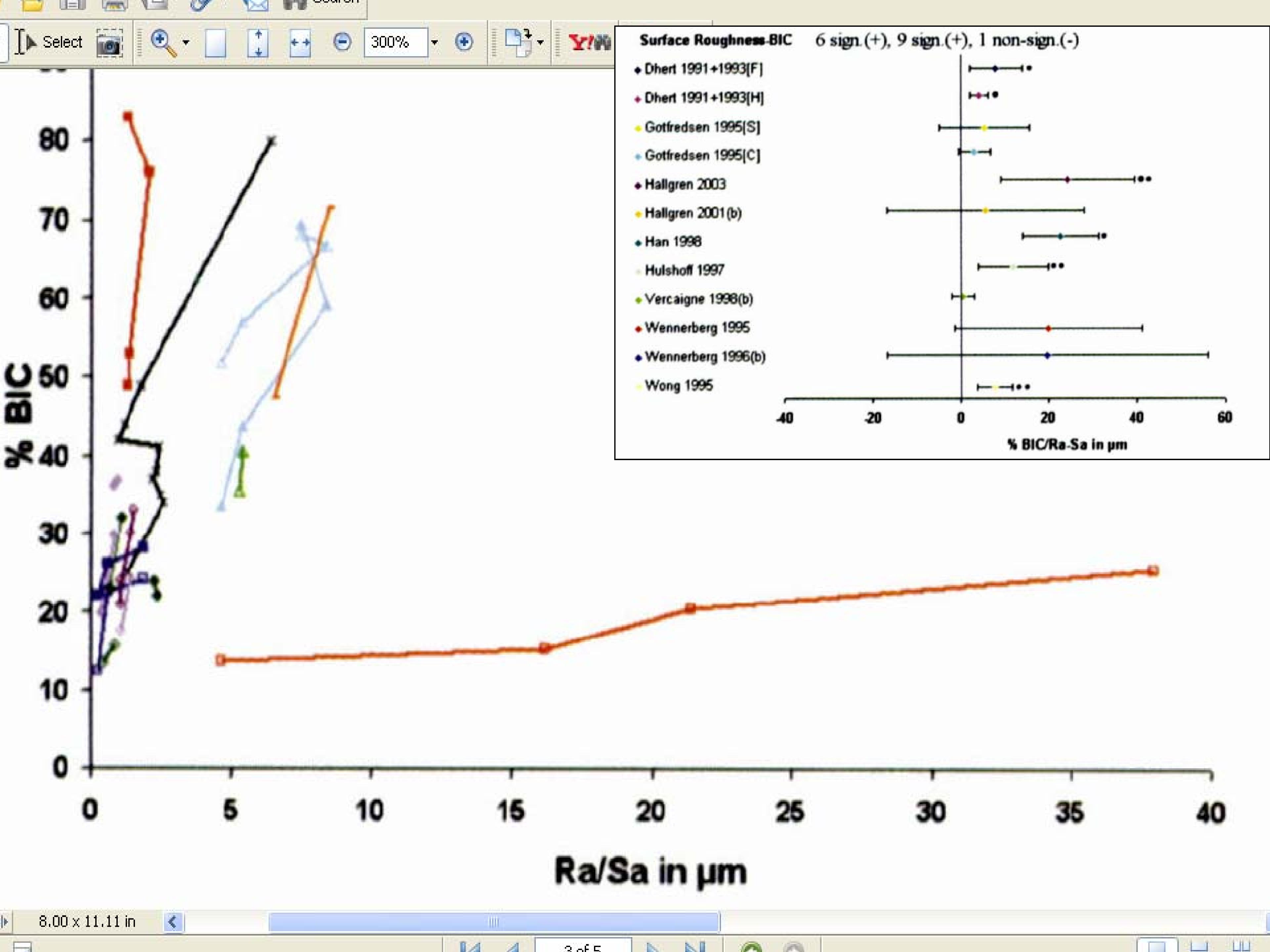
ABSTRACT

A systematic review was performed on studies investigating the effects of implant surface roughness on bone response and implant fixation. We searched the

INTRODUCTION

A major parameter for the clinical success of endosseous implant therapy is the formation of a direct contact between implant and surrounding bone. The implant-bone response is thought to be influenced by implant surface topography. As a consequence, over the last 20 years, a large number of implant systems with different surface topographies have been introduced. The literature on this topic is extensive and continuously increasing (Table 1). However, the claims made in numerous publications about the effect of implant surface roughness on bone response are not as straightforward as suggested. For example, there is a lack of agreement in findings from *in vivo* animal experiments, where the clinical performance of micro-roughened titanium implants is described on the basis of mechanical failure tests and histological considerations. Some of the studies indicated a tendency for an increase of bone-to-implant contact with increasing roughness of the implant surface (Buser *et al.*, 1991), while other studies either



Select
300%
Surface Roughness-BIC
6 sign.(+), 9 sign.(+), 1 non-sign.(-)
Dhert 1991+1993[F]
Dhert 1991+1993[H]
Gotfredsen 1995[S]
Gotfredsen 1995[C]
Hallgren 2003
Hallgren 2001(b)
Han 1998
Hulshoff 1997
Vercaigne 1998(b)
Wennerberg 1995
Wennerberg 1996(b)
Wong 1995
-40
-20
0
20
40
60
% BIC/Ra-Sa in µm
% BIC
0
10
20
30
40
50
60
70
80
0
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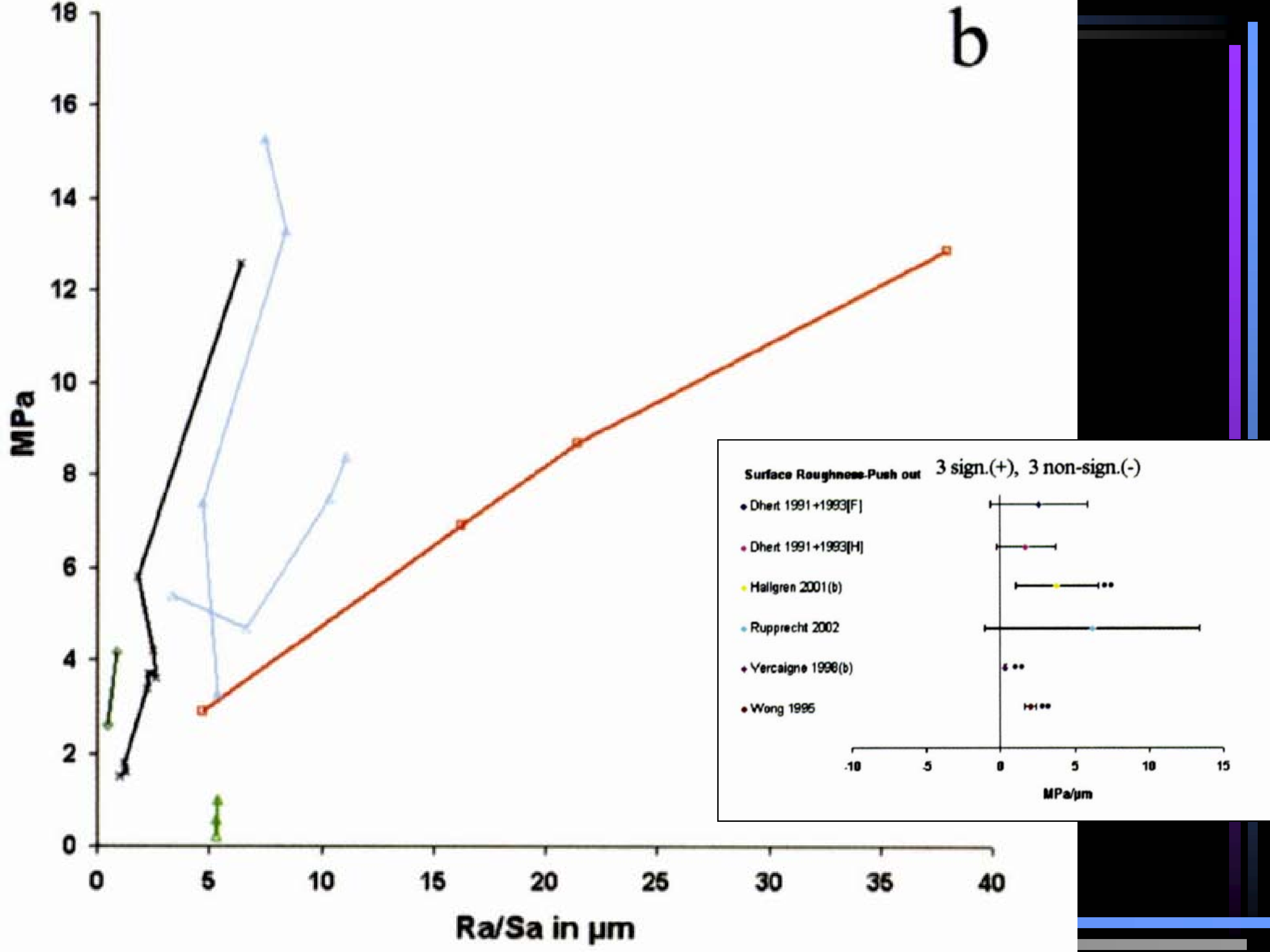
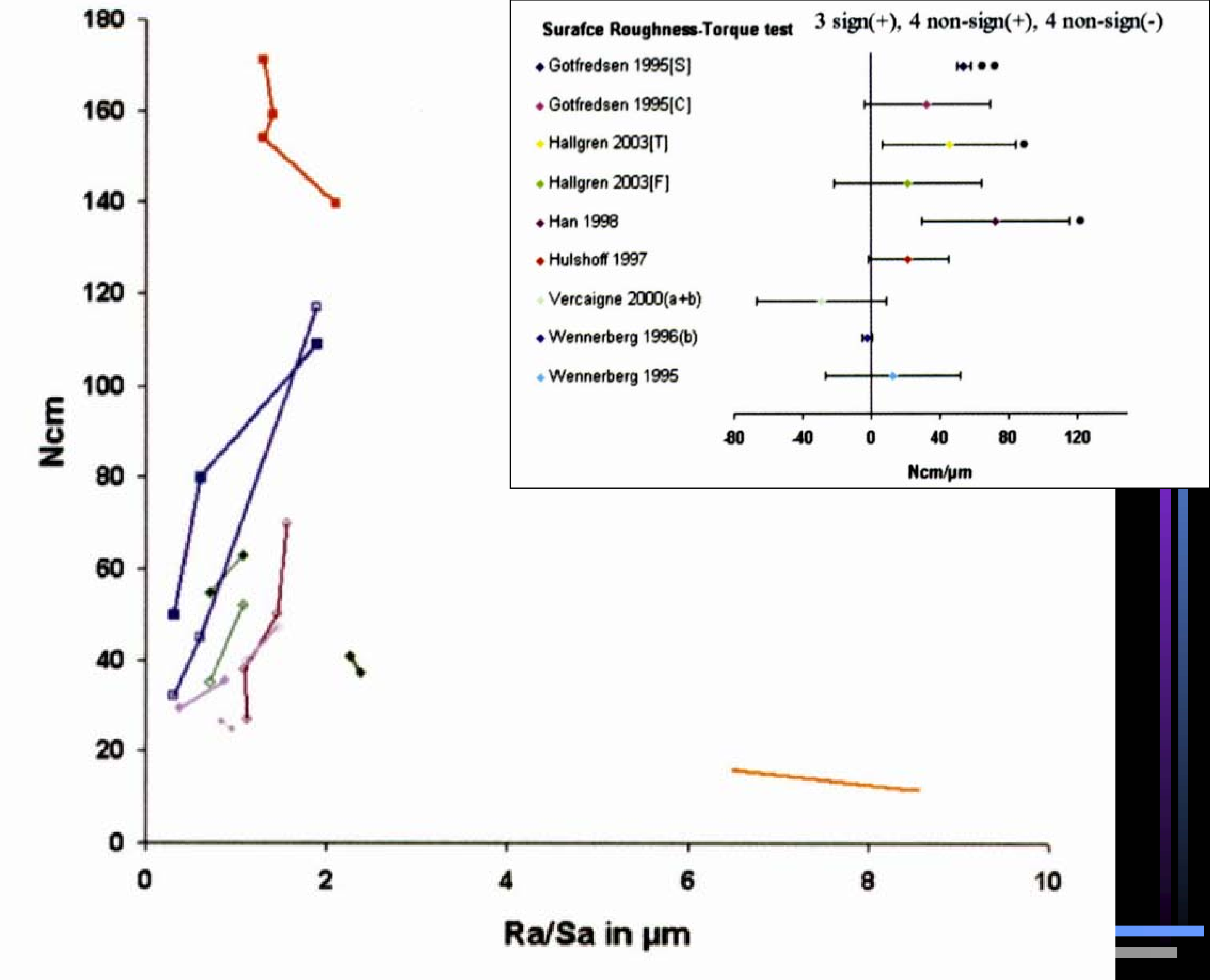
35
40
Ra/Sa in µm
8.00 x 11.11 in
3 of 5



b
MPa
18
16
14
12
10
8
6
4
2
0
0
5
10
15
20
25
30
35
40
Ra/Sa in µm
Surface Roughness-Push out
3 sign.(+), 3 non-sign.(-)
Dhert 1991+1993[F]
Dhert 1991+1993[H]
Hallgren 2001(b)
Rupprecht 2002
Vercaigne 1998(b)
Wong 1995
-10
-5
0
5
10
15
MPa/µm


Surafce Roughness-Torque test
3 sign(+), 4 non-sign(+), 4 non-sign(-)
Gotfredsen 1995[S]
Gotfredsen 1995[C]
Hallgren 2003[T]
Hallgren 2003[F]
Han 1998
Hulshoff 1997
Vercaigne 2000(a+b)
Wennerberg 1996(b)
Wennerberg 1995
-80
-40
0
40
80
120
Ncm/µm
Ncm
0
20
40
60
80
100
120
140
160
180
0
2
4
6
8
10
Ra/Sa in µm

Shalabi et al., J Dent Res 2006

Conclusions

- Almost all papers showed an enhanced bone-to-implant contact with increasing surface roughness.
- Six comparisons were significantly positive for the relationship of bone-to-implant contact and surface roughness.
- Also, a significant relation was found between push-out strength and surface roughness.
- Unfortunately, the eventually selected studies were too heterogeneous for inference of data

Relevance animal models *vz.* longitudinal trial results?

- Surface topography description?
- Model used?
- Roughness characterization?
- Measuring device?
- Consistency of results?
- Surgical technique for placement?