An Overview of Silicon Nitride as a Novel Biomaterial

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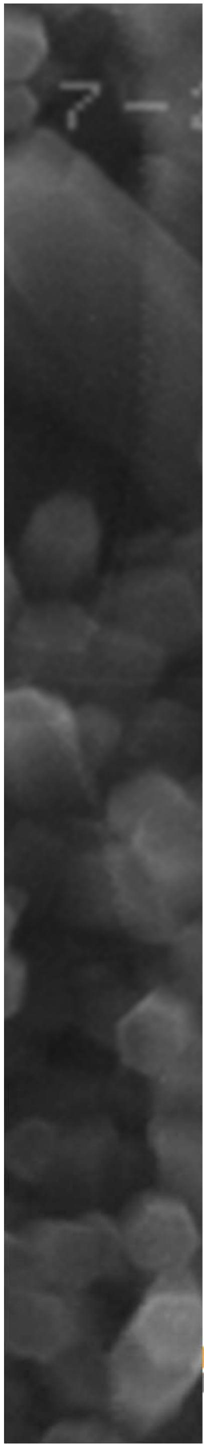


Si_3N_4 has many industrial uses

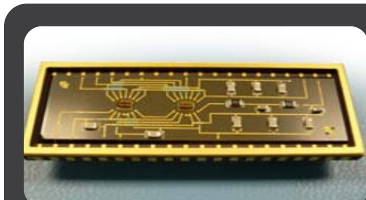
Bearings

- Machine tool spindles
- Dental handpieces
- Space shuttle/satellites
- Bicycles/in-line skates

Cutting tools

Turbo-machinery

- Turbine rotors
- Stators
- Glow plugs



Electronics

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Si_3N_4 medical applications

Spine

- Cages and corpectomy devices

Reconstructive

- Total joint arthroplasty

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Si_3N_4 Advantages

- High flexural strength
- High fracture toughness
- Reasonable Weibull modulus
- Low wear rate
- Biocompatible
- Possesses antibacterial behavior
- Textured or highly polished surfaces
- Allows for bone on-growth
- Allows for bone in-growth
- Phase stable composition – Immune to hydrothermal degradation

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Si_3N_4 Advantages

Comparative Properties of Biomaterials[1]

Property	Units	Si_3N_4	Al_2O_3	ZTA	YSZ	CoCr	PEEK Optima®	Ti - Alloy	Cortical Bone
Density	g/cc	3.15-3.26	3.986	4.37	6.04	~8.5	1.29	4.43	1.85
Elastic Modulus	GPa	300-320	400-450	350	210	210-250	4.2	105-115	12-Aug
Compressive Strength	MPa	2500-3000	2000-5000	4300	2200	600-1800	130-140	950-990	130-190
Flexural Strength	MPa	800-1100	300-600	1000-1150	1050	-	160-180	-	-
Fracture Toughness	$MPa \cdot m^{1/2}$	8-11	4-5	5.7	10.5	50-100	-	75	-
Hardness	GPa	13-16	14-16	19.1	12.5	3-4	-	3.4	-
Surface Composition	NA	$SiNH_2$ & SiOH	Al_2O_3	ZrO_2,Al_2O_3	ZrO_2	CoO,Cr_2O_3	-OH Groups	TiO_2, Al_2O_3	$Ca_5(PO_4)_3(OH)$
Surface Charge at pH =	NA	Positive	Positive	Positive	Positive	Negative	Negative	Negative	-

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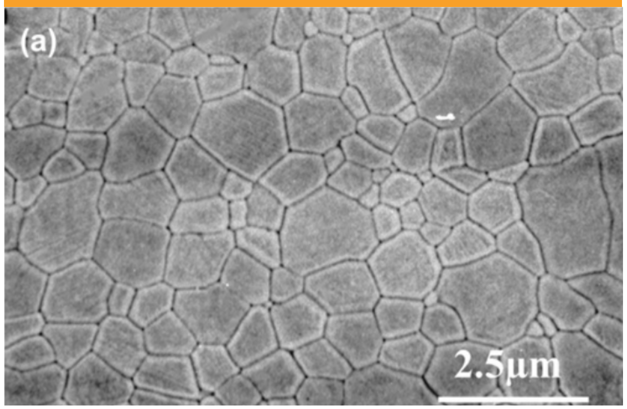
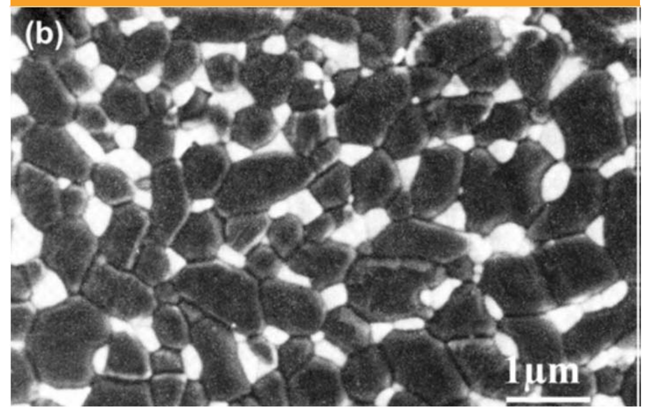
1. B. S. Bal, et al., "Orthopedic applications of silicon nitride ceramics," *Acta Biomaterialia*, 8, (2012), 2889-2898.

Bioceramic Microstructures

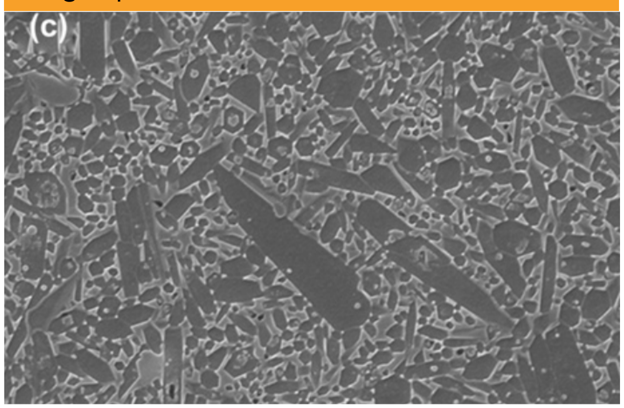
Al_2O_3 – Polished



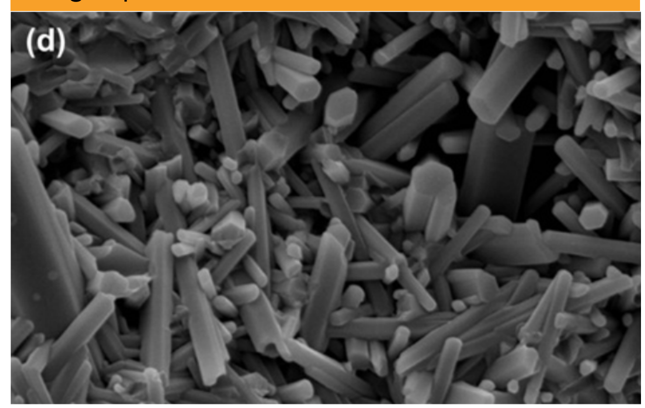
ZTA – Polished



Si_3N_4 – Polished



Si_3N_4 – As-Fired



Crack Propagation in Ceramics

Conventional ceramics

Low fracture toughness due to non-torturous crack path

A

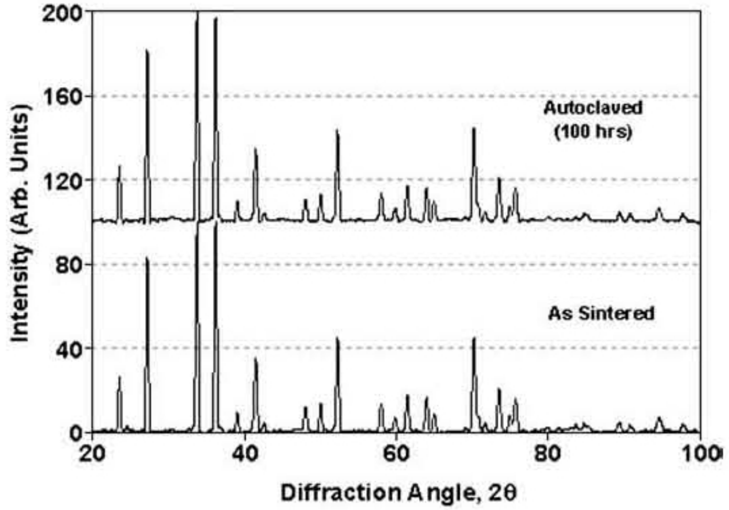
Si_3N_4ceramics

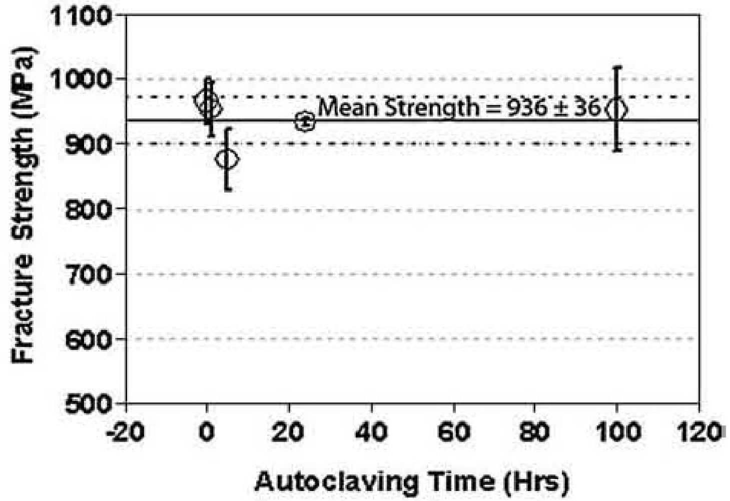
High fracture toughness results from a torturous crack path

B

Phase and Strength Stability of Si_3N_4

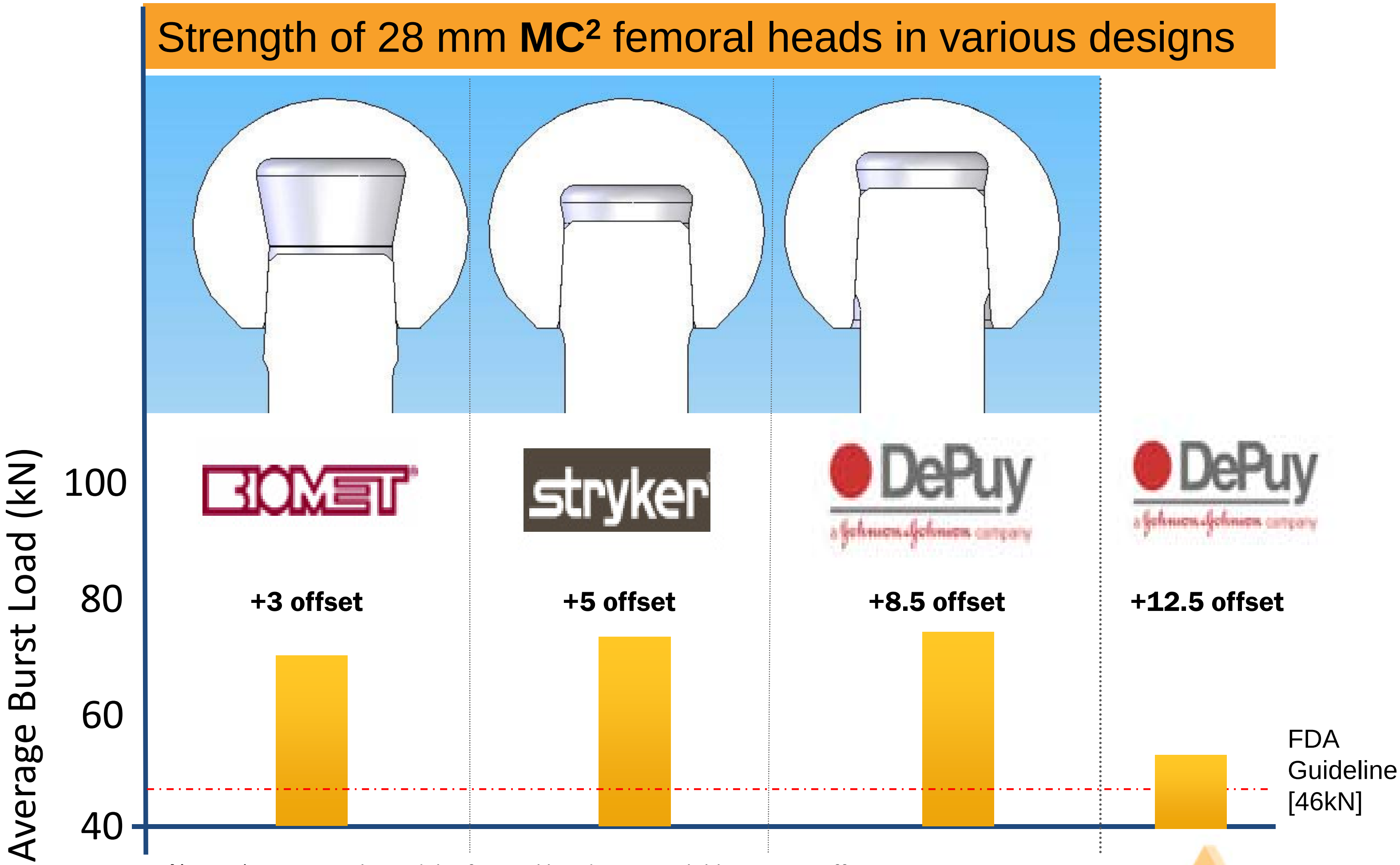
- Autoclave conditions: 120°C, 1 atm steam for up to 100 hrs
- No change in phase composition
- No change in flexural strength
- Inherently stable microstructure





B. S. Bal, et al., "Fabrication and Testing of Silicon Nitride Bearings in Total Hip Arthroplasty," *J. Arthroplasty*, 24, [1], 110-116, (2009).

Si_3N_4 Femoral Head Burst Test Results



Note: * 28mm Biolox™ *delta femoral heads not available in +12.5 offset*

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Si_3N_4 Biocompatibility

Si3N4 Biocompatibility Tests (ISO 10993)	Pass
Cytotoxicity	✓
Systemic Toxicity	✓
Sensitization	✓
Genotoxicity	✓
Hemolysis	✓
Muscle Implantation (2 & 4 wk.)	✓
Sterilization compatibility (steam and γ - irradiation)	✓

Confirmation

- Kue R, Sohrabi a, Nagle D, Frondoza C, Hungerford D., "Enhanced proliferation and osteocalcin production by human osteoblast-like MG63 cells on silicon nitride ceramic discs," *Biomaterials*. 1999;20(13):1195–201.
- Neumann A, Reske T, Held M, et al., "Comparative investigation of the biocompatibility of various silicon nitride ceramic qualities in vitro," *Journal of Materials Science. Materials in Medicine*. 2004;15(10):1135–40.

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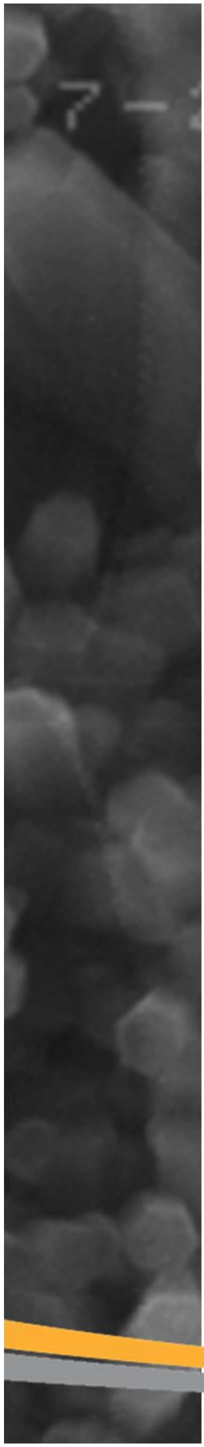
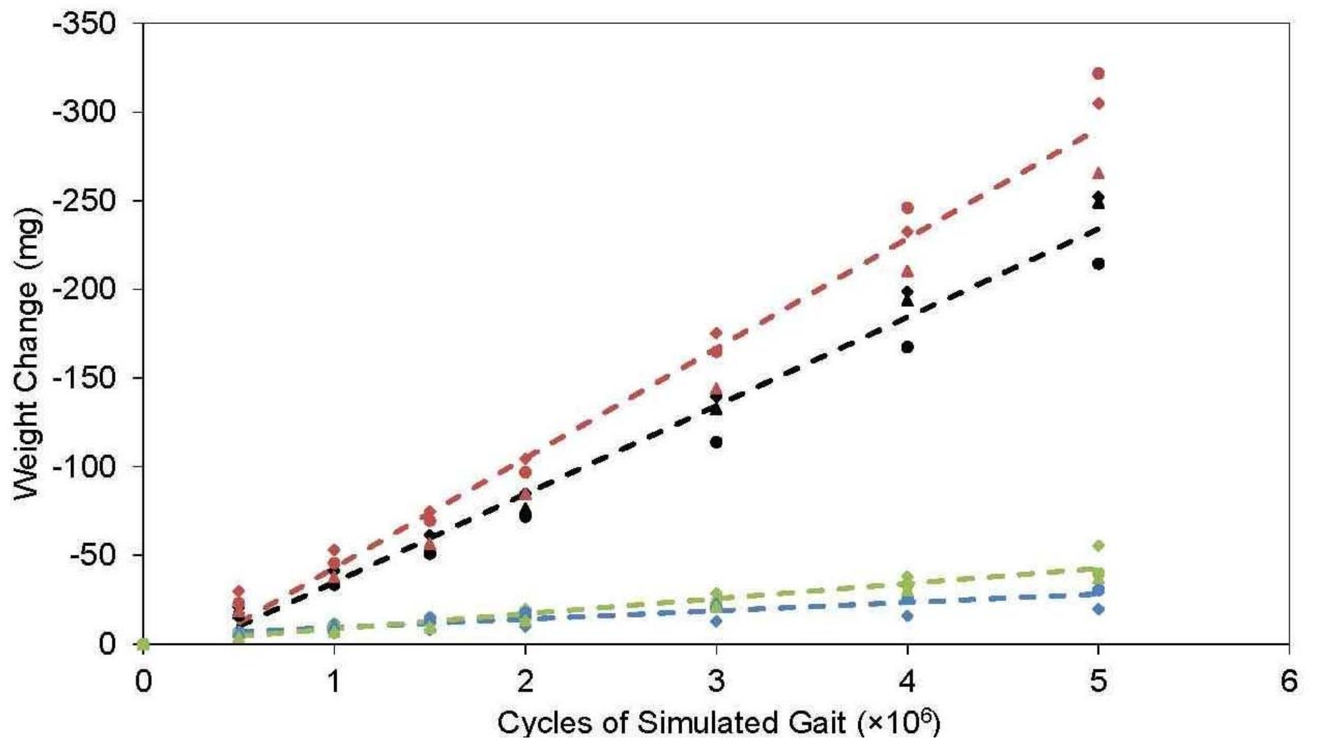


Si_3N_4 Wear Characteristics



28mm **PE/CoCr** #1-3	28mm **PE/SN** #1-3	28mm **XLPE/SN** #1-3	40mm **XLPE/SN** #1-3

B. J. McEntire, "Hip Simulator Wear Testing of Infinia® Femoral Heads,"
Amedica Internal Research Report #RR 10001-11 A-2, (June 17, 2012).

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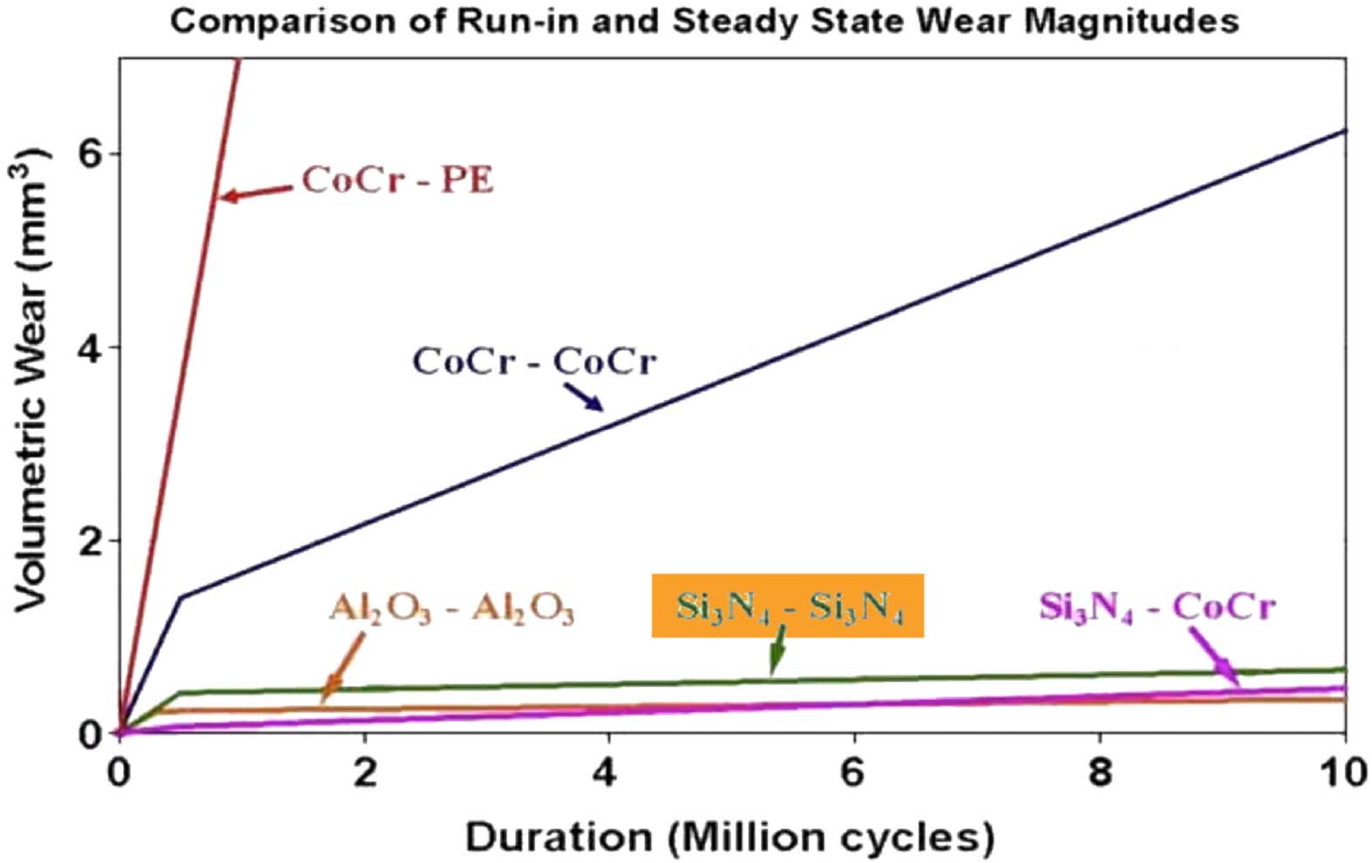
Si_3N_4 Wear Characteristics



B. S. Bal, et al., “Fabrication and Testing of Silicon Nitride Bearings in Total Hip Arthroplasty,” *J. Arthroplasty*, 2009;24(1):110-116.

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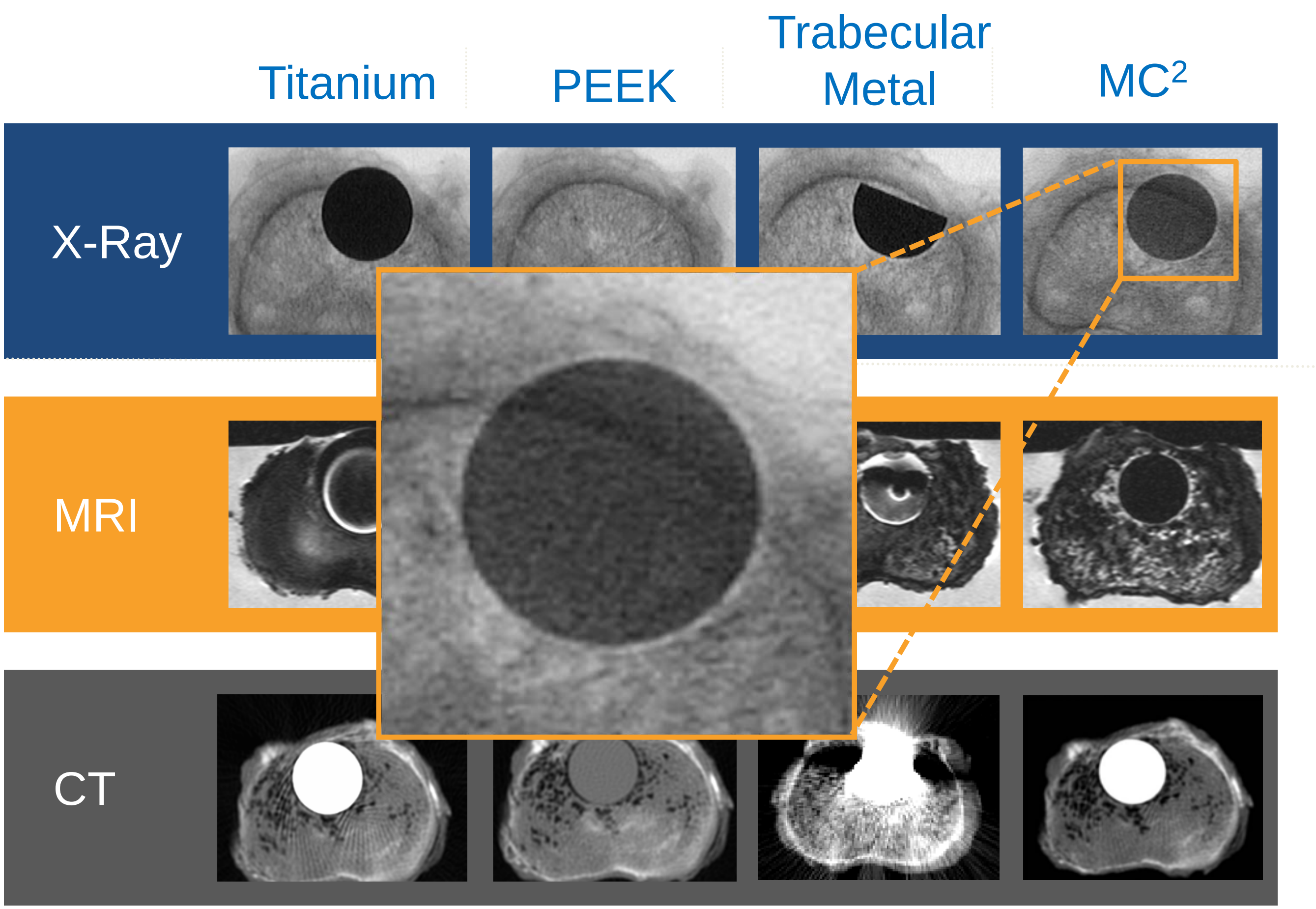
Si_3N_4 Imaging Characteristics



J. Bernero, et al., "Medical Imaging Characteristics of Silicon Nitride," *SAS Conference*, Miami, (2008).

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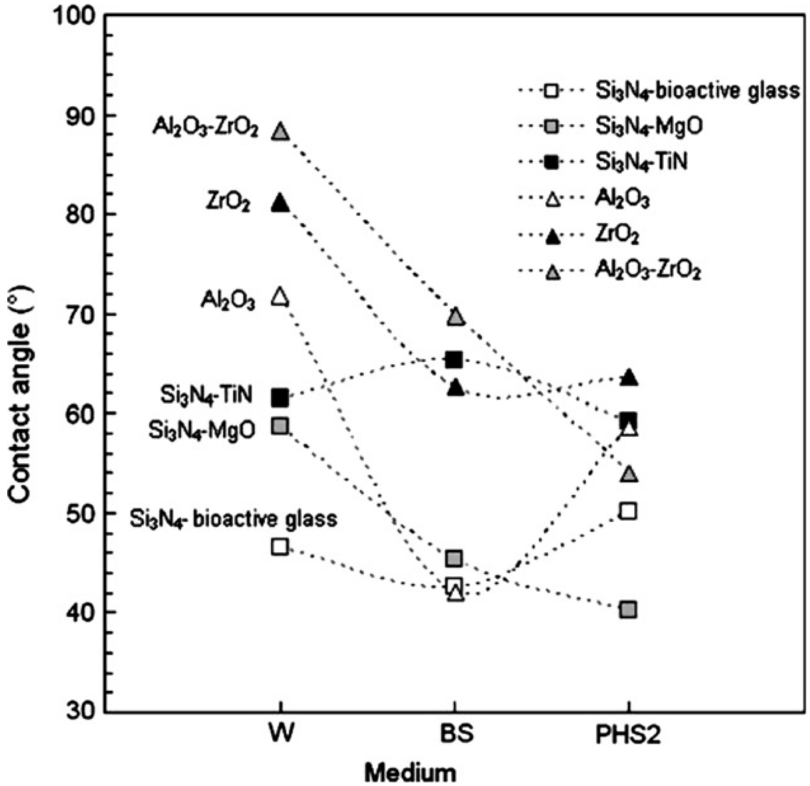
Wettability of Various Biomaterials

Contact Angle Measurements for Bioceramics[1]



Contact Angle Measurements for Biomaterials[2]

Material	Water Contact Angle
PEEK	95°
Titanium	76°
Si_3N_4	39°

W = Water; BS = Diluted Bovine Serum; PHS2 = Hank's Balanced Salt Solution

1. M. Mazzocchi et al., "On the possibility of silicon nitride as a ceramic for structural orthopaedic implants. Part II: Chemical stability and wear resistance in body environment," *J. Mater. Sci. Mater. Med.*, (2008);19:2889-2901.
2. D. Gorth et al., "Decreased bacteria activity on Si_3N_4 surfaces compared with PEEK or titanium," *Int. J. Nanomedicine*, (2012), in press.

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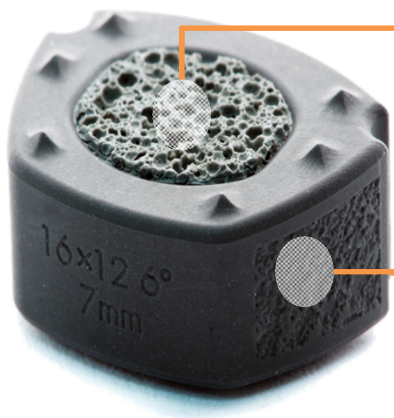
Porous and Dense Si_3N_4 Constructs

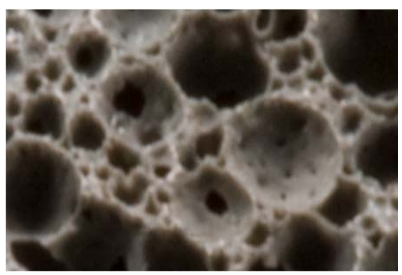


C^S^C®

Si_3N_4 Cancellous Structured Ceramic

MC² ®

Si_3N_4 Micro-Composite Ceramic



- Strength
- Superior Imaging
- Osteo-integration / Conductive Scaffold
- Bacterial Resistant Material

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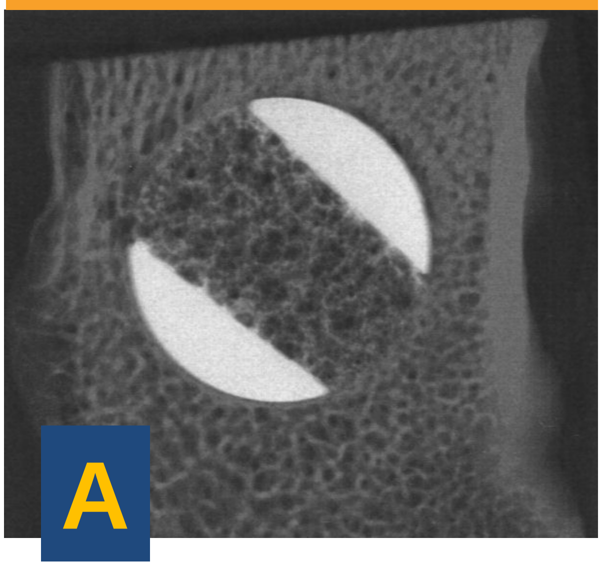
Bone Grows into C^{S}C® Si_3N_4

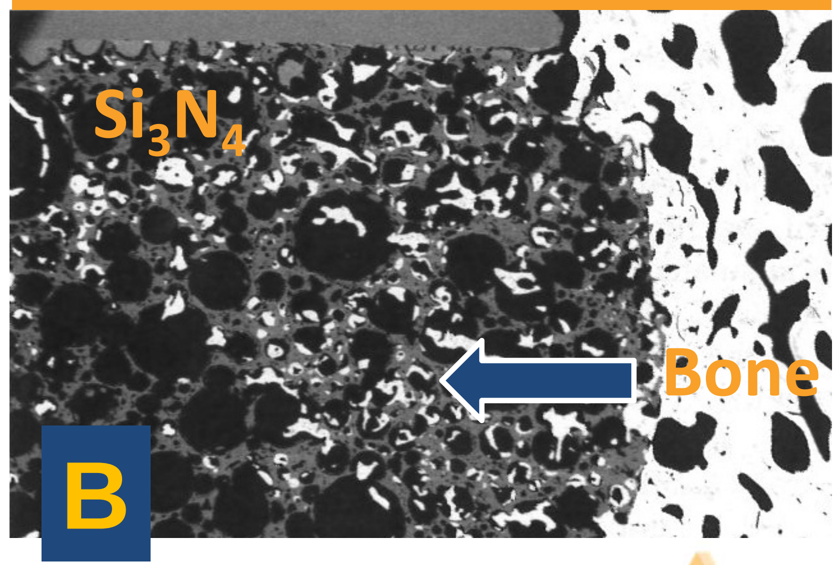
Sheep Study – Medial femoral condyle

(Cancelleous Structured Ceramic (C^{S}C®), ~72% Porous Si_3N_4 Construct)

Retrieved implant
12 wks post-op



Bone penetrated >3mm
into CSC®



M. C. Anderson, et al., "Bone In-Growth into Porous Silicon Nitride," *J. Biomed. Mat.*, *Part A,* (2010);92A(4);1598-1605.

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Clinical Results of C^S^C® Si_3N_4

- Currently Used as an Implant in the EU
  - One Level Cervical Fusion Without Instrumented Fixation
  - Excellent Fusion and Osteointegration

MRI – Three Months Post-Operatively

Mark P. Arts, MD, PhD, Neurosurgeon, *Medical Center Haaglanden*, The Netherlands, Personal Communication, (May, 2012)

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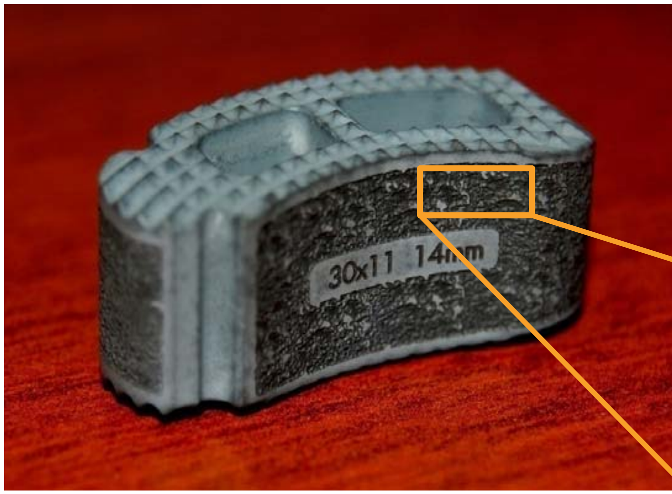
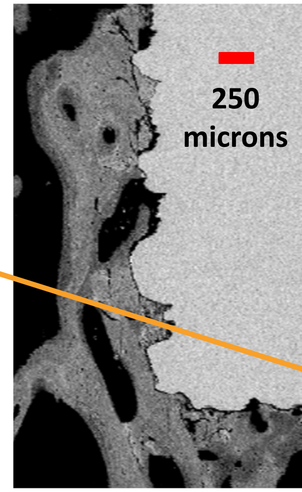
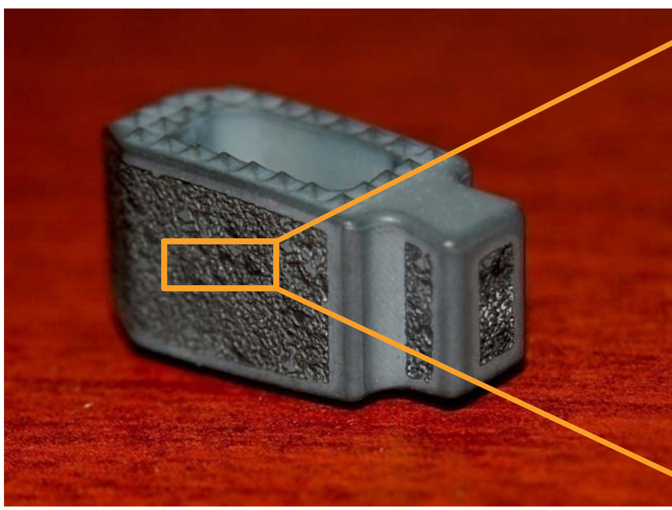
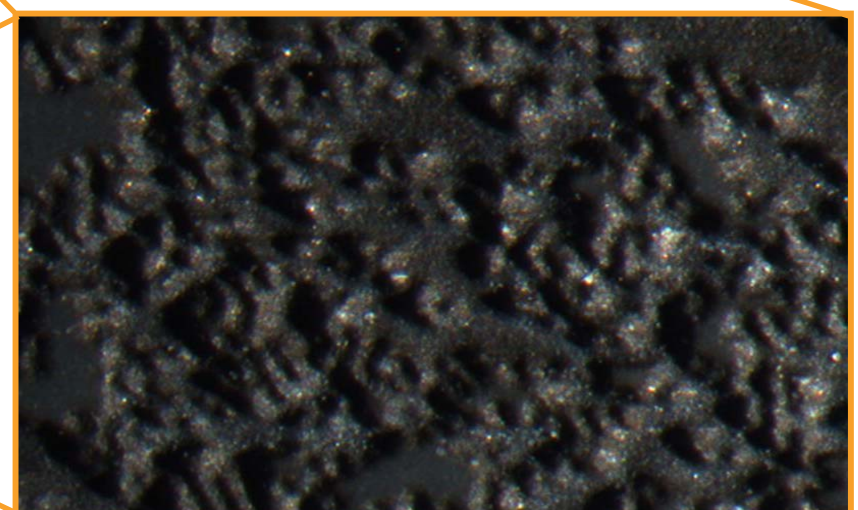
Texturing Leads to Osteointegration





- Micro-roughened surface
- Increases surface area for on-growth
- Inter-digitated bony fixation





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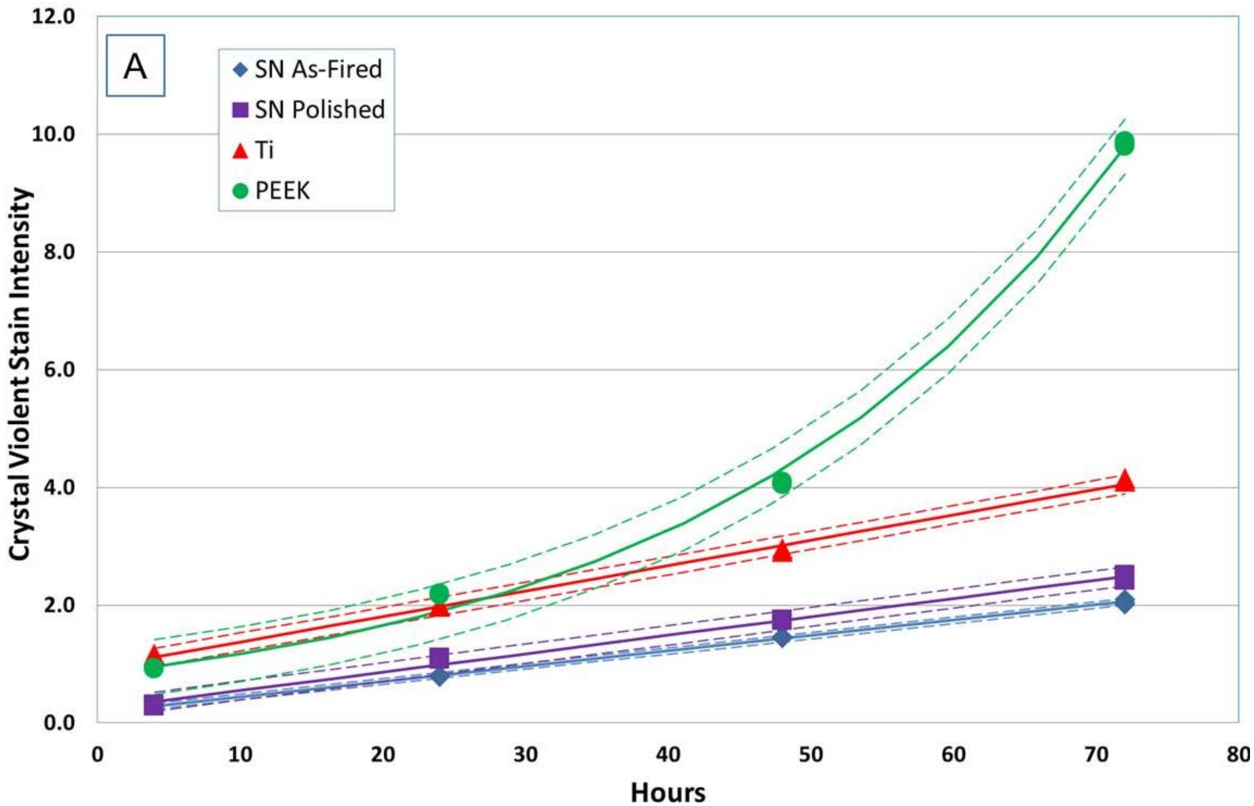
Anti-Infective Properties of Si_3N_4

In vitro studies

Staph. epi Biofilm Production[1]

(Five strains of bacteria examined on three biomaterials)



1. D. Gorth et al., "Decreased bacteria activity on Si_3N_4 surfaces compared with PEEK or titanium," *Int. J. Nanomedicine*, (2012), in press.

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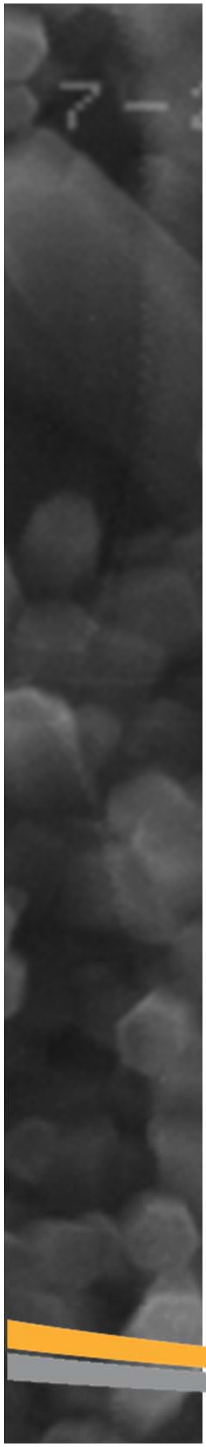
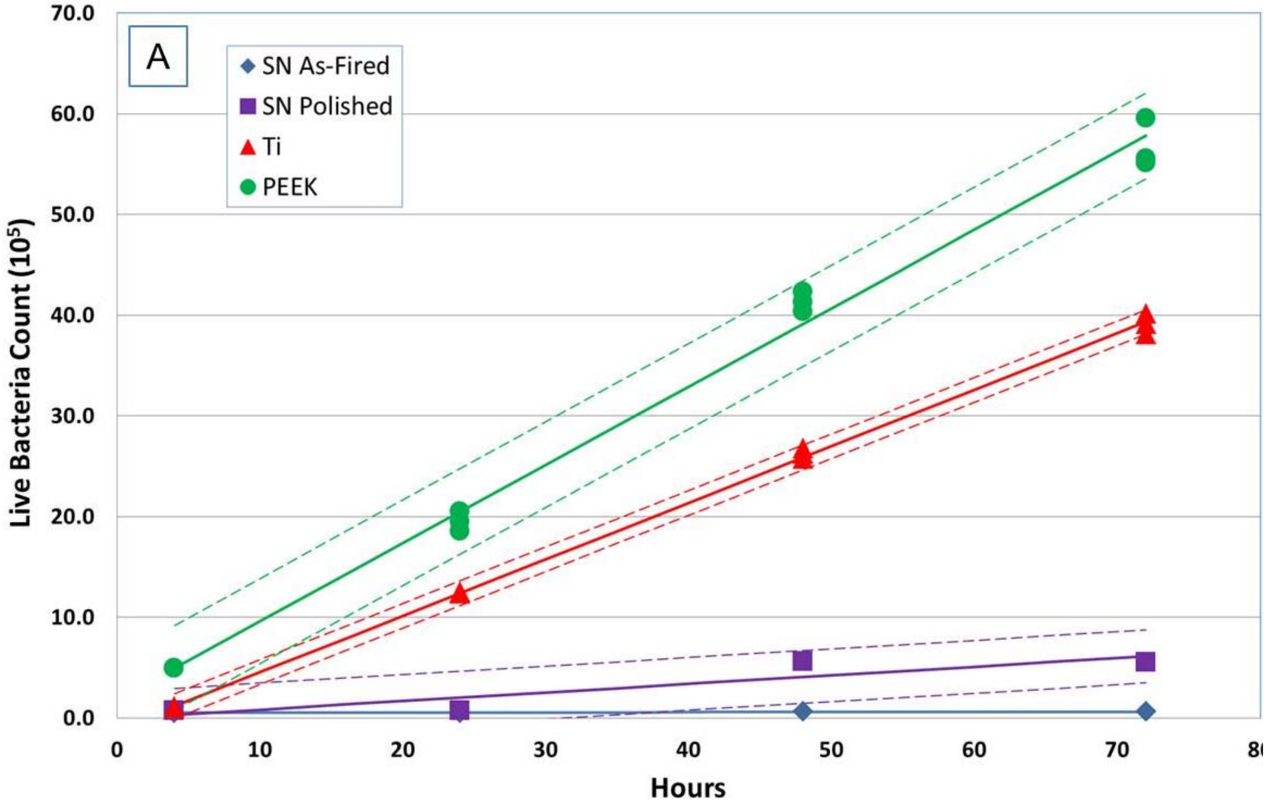


Anti-Infective Properties of Si_3N_4

In vitro studies

Staph. epi Count of Live Bacteria[1]

(Si_3N_4 demonstrates remarkable resistance to biofilm formation and growth)



1. D. Gorth et al., "Decreased bacteria activity on Si_3N_4 surfaces compared with PEEK or titanium," *Int. J. Nanomedicine*, (2012), in press.

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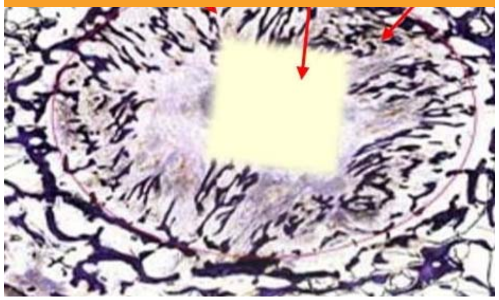
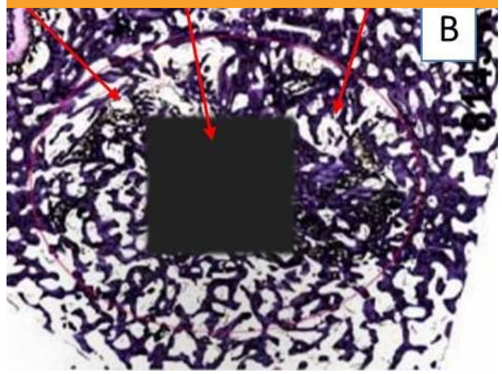
In vivo Wistar Rat Calvarial Study[1]

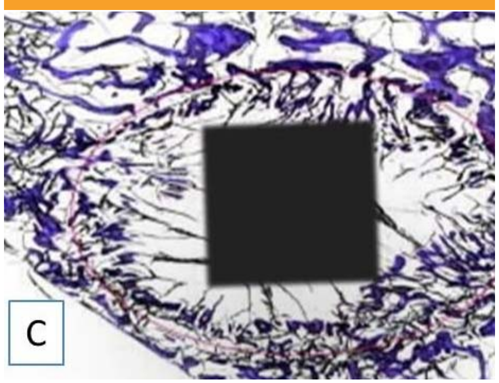
PEEK - 5% new bone and 95% bacteria at implant interface; 21% new bone growth and 88% bacteria growth in surgical area



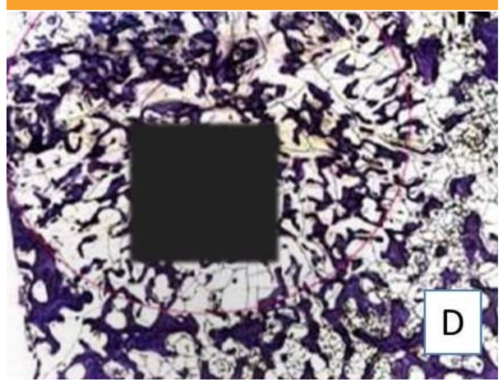
Si_3N_4 – 65% new bone at implant interface, 71% new bone in surgical area



Ti – 19% new bone at implant interface, 36% new bone in surgical area



Si_3N_4 – 52% new bone at implant interface, 66% new bone in surgical area



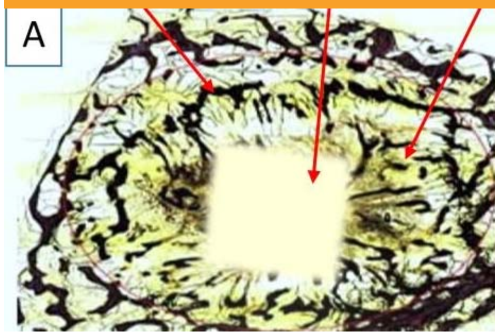
Histology

3 months post-operatively. no bacteria inoculation

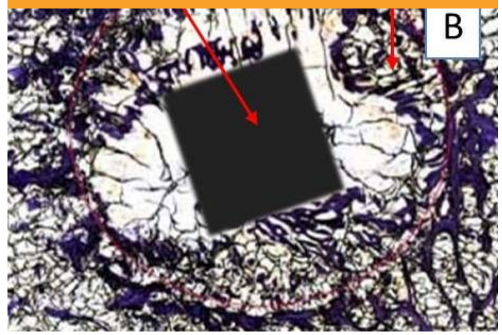
1. T. J. Webster et al., "Anti-infective and osteointegration properties of silicon nitride, poly(ether ether ketone), and titanium implants, *Acta Biomaterialia*, (2012), in press.

In vivo Wistar Rat Calvarial Study[1]

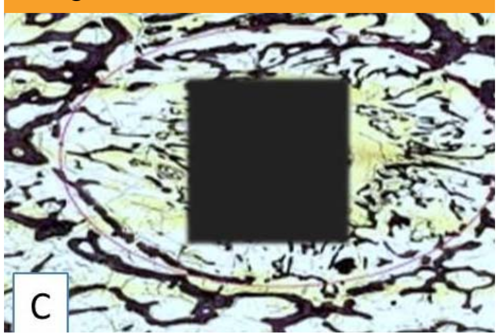
PEEK - 8% new bone at implant interface, 24% new bone in surgical area



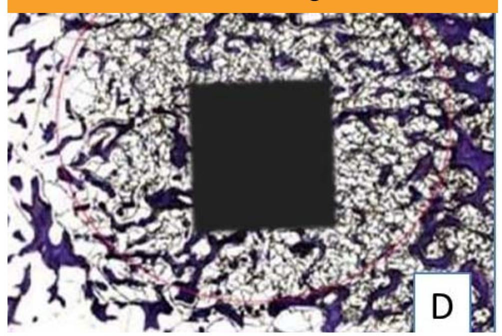
Si_3N_4 - 25% new bone and 0% bacteria at implant interface, 39% new bone growth and 0% bacteria in surgical area



Ti – 9% bone and 67% bacteria at implant interface, 26% new bone and 21% bacteria in surgical area



Si_3N_4 – 21% new bone and 0% bacteria at implant interface, 42% new bone and 0% bacteria in surgical area



Histology

3 months post-operatively with 10^4 *S. epi.* bacteria inoculation

1. T. J. Webster et al., “Anti-infective and osteointegration properties of silicon nitride, poly(ether ether ketone), and titanium implants, *Acta Biomaterialia*, (2012), in press.

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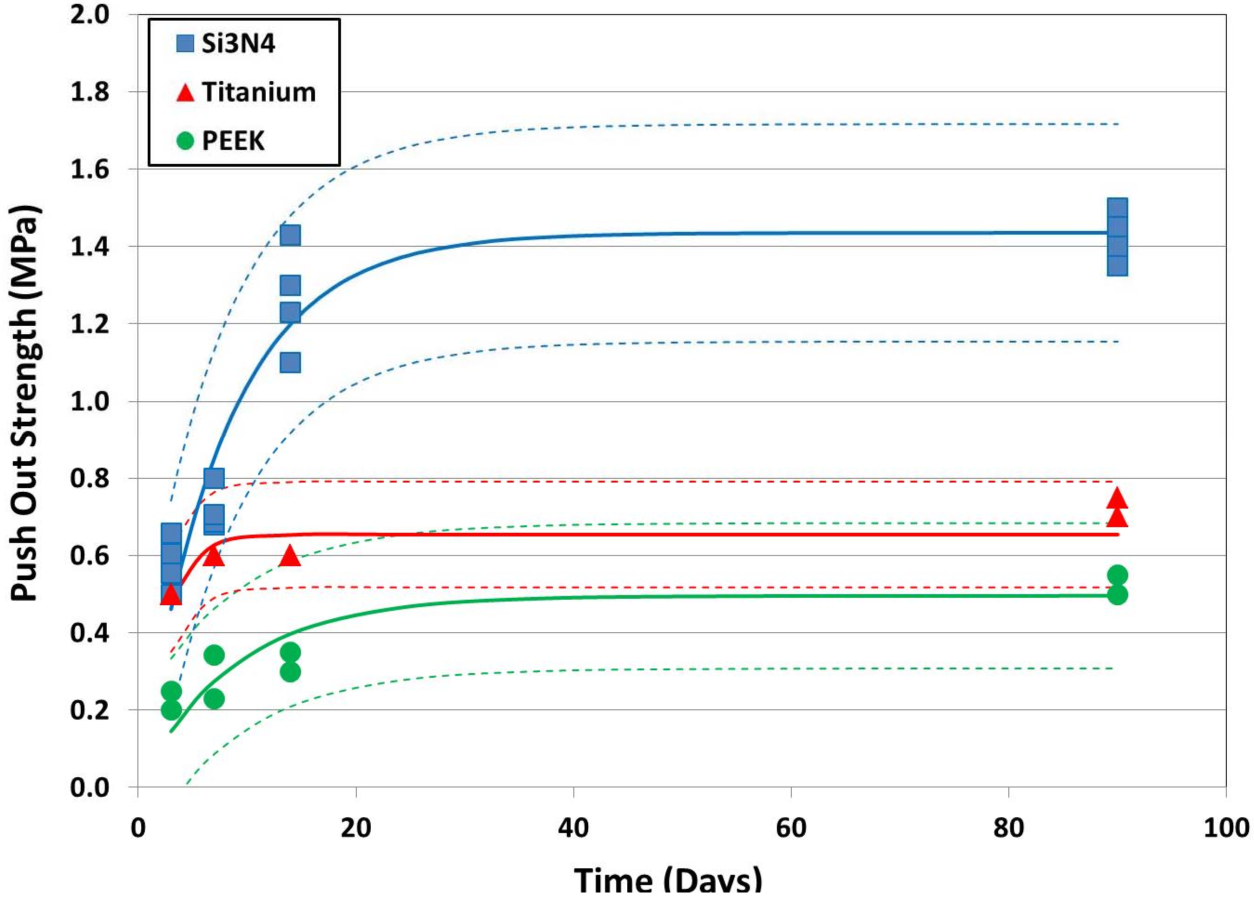
In vivo Wistar Rat Calvarial Study[1]

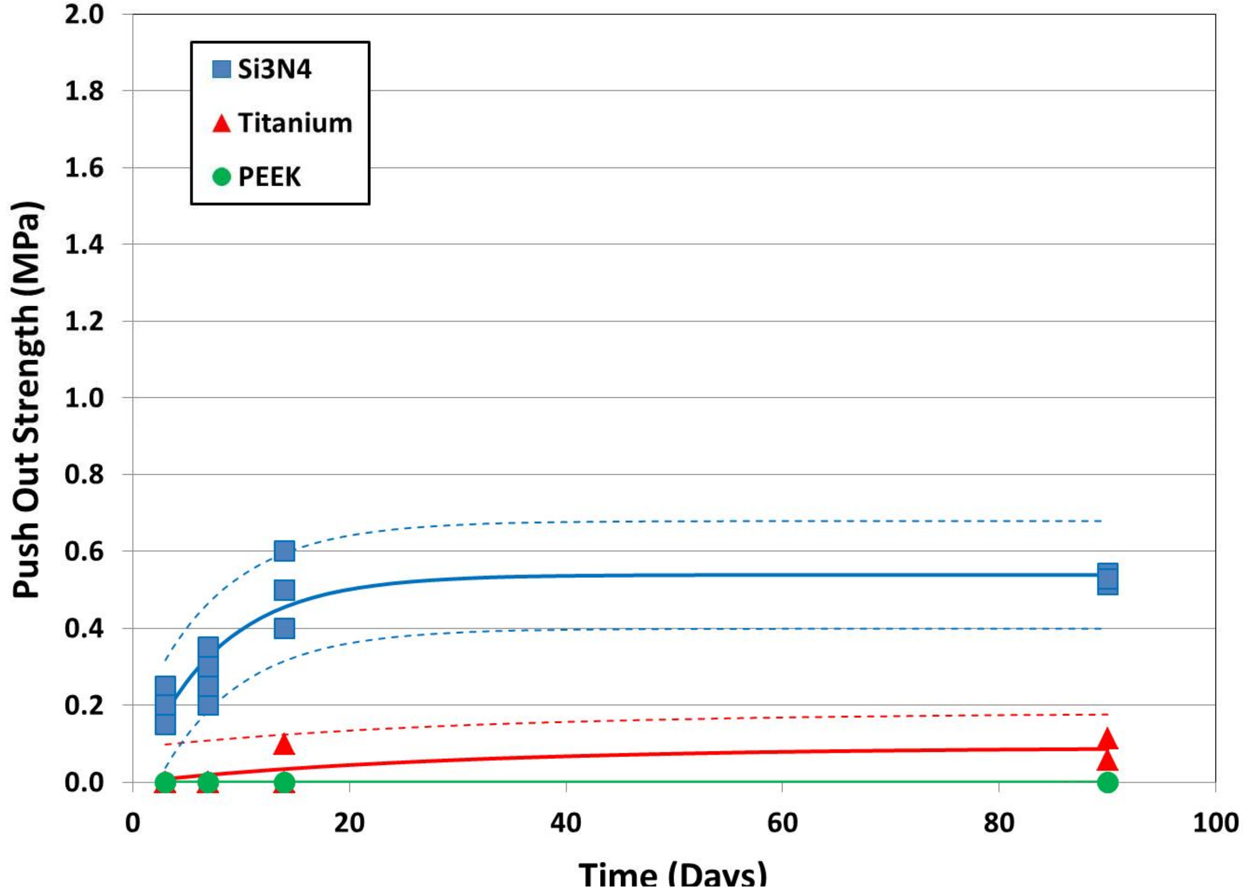
Push-out strengths without bacteria inoculation



1. T. J. Webster et al., “Anti-infective and osteointegration properties of silicon nitride, poly(ether ether ketone), and titanium implants, *Acta Biomaterialia*, (2012), in press.

In vivo Wistar Rat Calvarial Study[1]

Push-out strengths **with** 10^4 *Staph. epi.* inoculation



1. T. J. Webster et al., "Anti-infective and osteointegration properties of silicon nitride, poly(ether ether ketone), and titanium implants, *Acta Biomaterialia*, (2012), in press.

A M E D I C A

Summary

Si_3N_4

- High flexural strength and phase stability
- High fracture toughness; Resists cracking and stress risers
- Chemically stable; Resistant to biodegradation
- Biologically inert; biocompatible
- Highly wear resistant; Low wear rates
- Possesses optimal imaging qualities
- Excellent wettability to biologic fluids
- Good bone *in-growth* in the form of CSC®
- Good bone *on-growth* in the form of *MC²*®
- Leads to bone apposition instead of a fibrous layer
- Possesses inherent anti-infective characteristics

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