Slow Release Anti-bacterial and Hard-wearing Orthopedic Prosthetics Coating

NCCVAS Junction Tech UG

Babak Adibi - December 2022

SURFION

Joint damage due to wear & tear and arthritis

Joint replacement improve quality of life

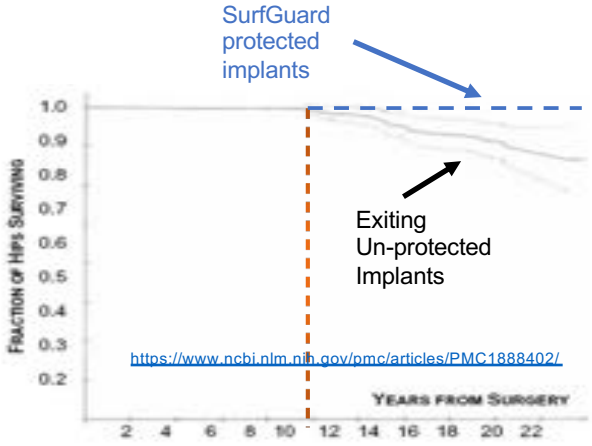
2.5M joint replacements per year in US

Orthopedic Arthroplasty Failure – Infection and Wear

- Periprosthetic Joint infection (PJI)
  - ~ 5 % PJI → Revision Arthroplasty
    - Much patient discomfort and cost
  - – $1.2B cost Impact per year (2020)

Categories	Devices	Infection Occurrences
Cardiac Devices (%)	Intra-aortic balloon pump	0.08–0.13%
	Left ventricular assist device	16–36%
	Heart valve	7–15%
	Cardiac implantable e-devices	5–20%
Prosthetics Joints (%)	Shoulder	1.2%
	Hip	1–2%
	Knee	1–4%
	Elbow	5%

- Short lifetime due to Wear
  - – Longer and active life need 25+ years
    - Typical implant life ~10+ years
  - – Metal alloy joint wear 1.2mm/10 years
    - Wear → Particle generation



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5110396/
Based on 2.5 Million Implants in US
https://www.drugwatch.com/hip-replacement/surgery/
J. Scott VanEpps et al Shock: 2016; 46(6): 597-608
https://www.hss.edu/conditions_revision-total-hip-replacement-overview.asp
S kurtz et al J of Arthroplasty, **27**, 8, Supp, 61-65, E1

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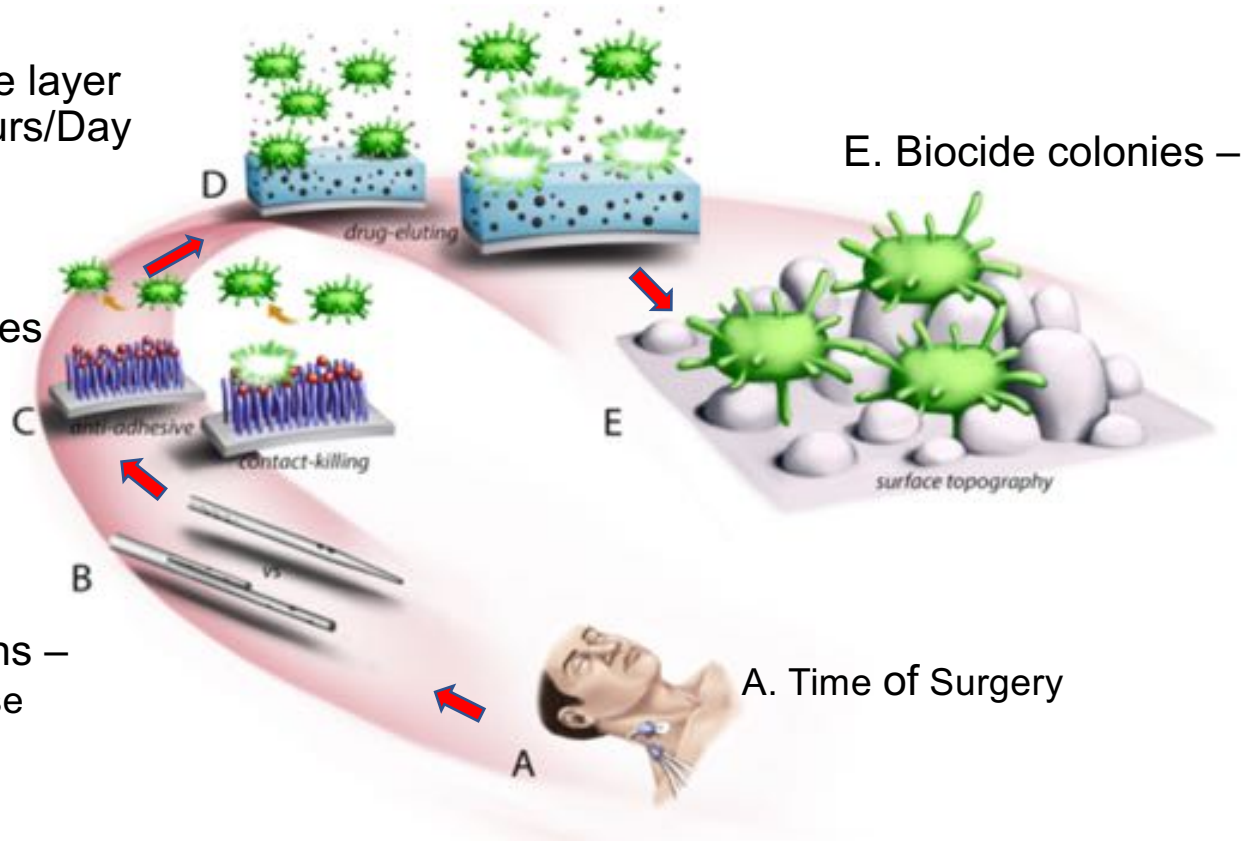
Infection Progression Post Surgery

D. Nano-Biocide layer formation – Hours/Day

E. Biocide colonies – Days/Weeks

C. Biocide Attack – Minutes



B. Instrumentations – Forced One time use

A. Time of Surgery

Pictorial strategy – J. Scott VanEpps et al Shock: 2016; 46(6): 597-608

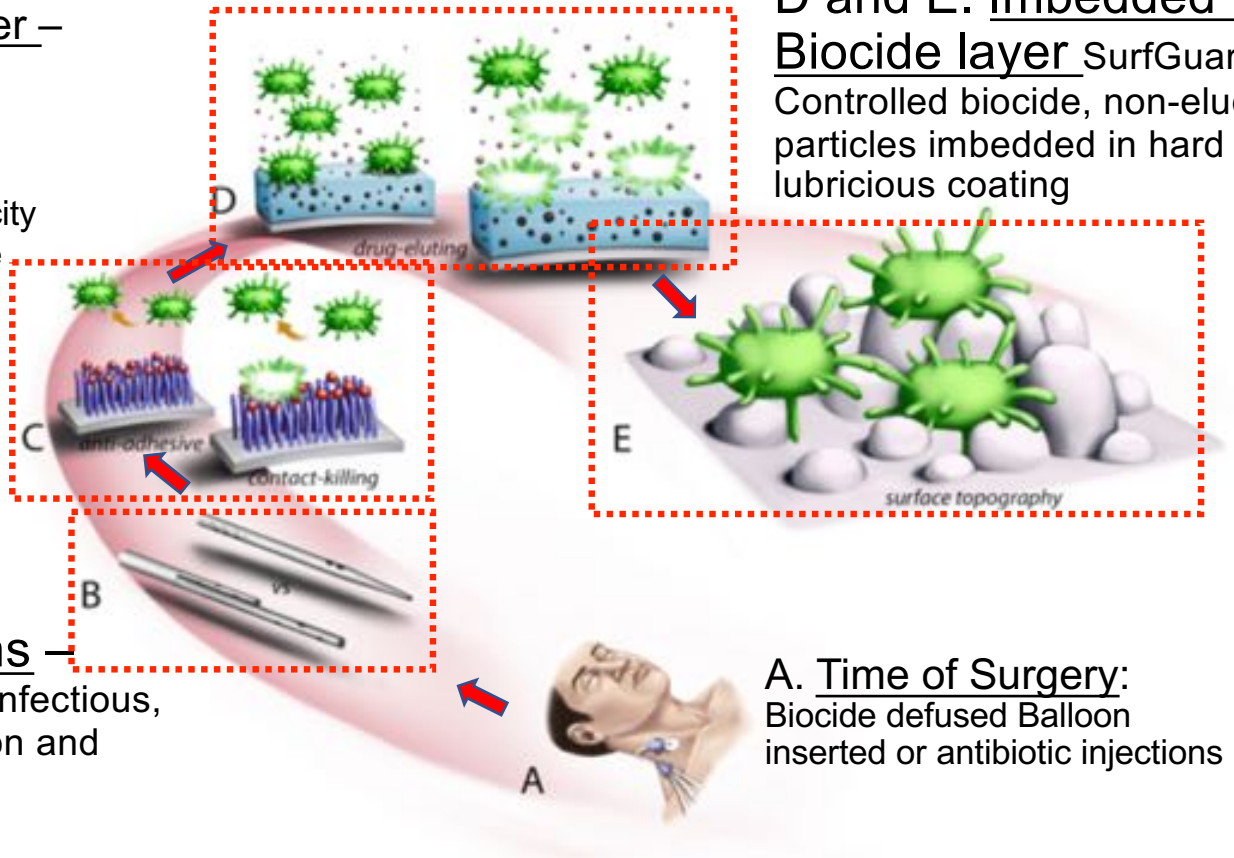
Anti-Infection Techniques and Competitive Solutions

C. Biocide Surface Layer –

Temporary and Cytotoxicity.

Exiting Solutions:

- Agluna → Hi Cytotoxicity
- Implantcast,→ Hi Cytotoxicity
- Hydroxyapatite → short life
- N2 → none anti-infectious



D and E. Imbedded Nano-Biocide layer SurfGuard long lasting, Controlled biocide, non-eluding, Nano-particles imbedded in hard wearing lubricious coating

B. Instrumentations –

SurfGurad provide anti-infectious, lubricious instrumentation and ease of cleaning

A. Time of Surgery:

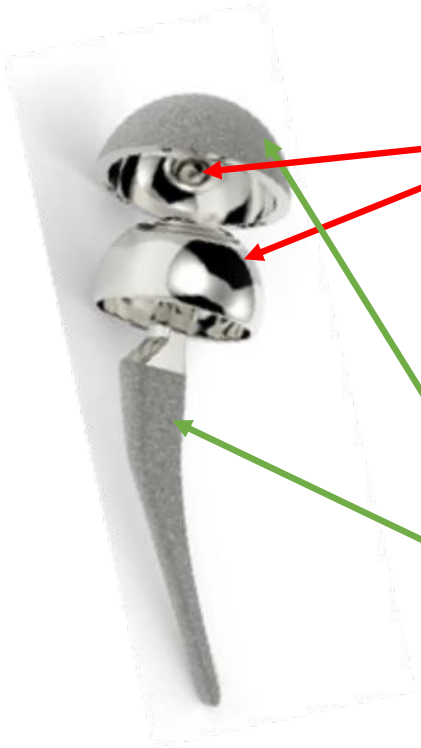
Biocide defused Balloon inserted or antibiotic injections

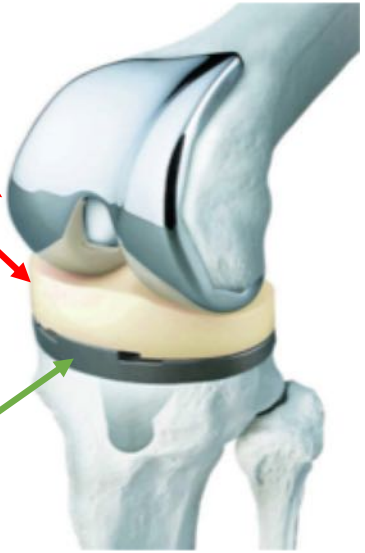
Pictorial strategy – J. Scott VanEpps et al Shock: 2016; 46(6): 597-608

SurfGuard™ Protecting Prosthetic Surfaces

Articulating

- **Hard Wearing**
  - High lubricity
- **Anti microbial**
  - Minimal cytotoxicity

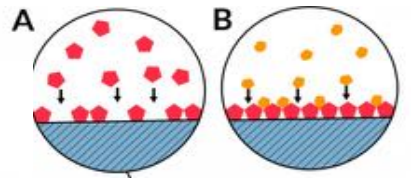




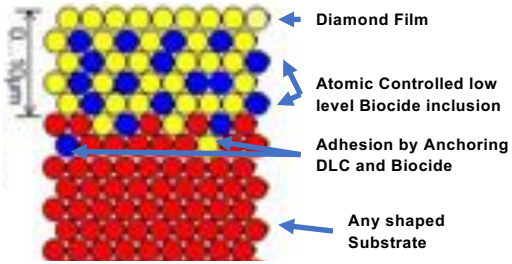
None - Articulating

- **Anti microbial**
  - Minimal Cytotoxicity
- **Osseointegration**
  - Hydrophobic surface

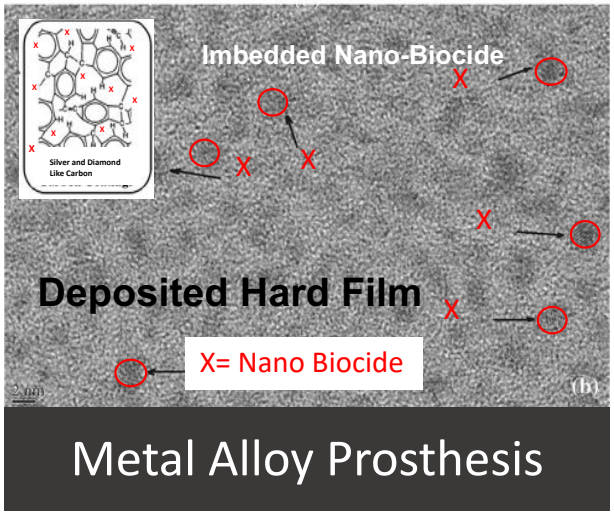
SurfGuard - Biocide + Diamond Film Formation



Mix two different materials – Deposition and Implantation



One step very controlled mixing of multiple elements – Biocide (Ag) + Diamond film



Nano Biocidal Film Technology

Patents:-
Film and Equipment 17/185,714
Equipment 62/983,625
Film 62/983,711
Equipment 62/724,026

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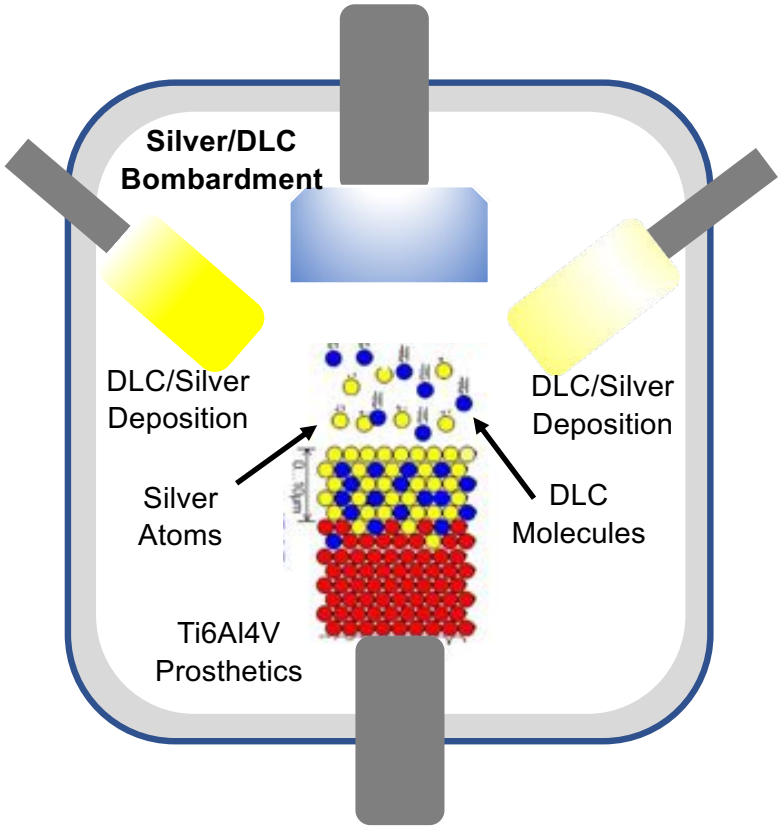
Combined Bombardment and Deposition system



Continuous Nano- antimicrobial elements throughout the film

Improved wear rate due to Hardwearing film and biocide bombardment

Conformal deposition for complex shapes and all materials and biocides

Anti-infectious In Vitro testing requirements

Parameter	Specific Requirements[1]
Antimicrobial release	Eluate volume and fluid exchange protocols; Total amount and concentration of antibacterial agent incorporated.
Antibacterial activity	Testing against a panel of pathogens reflecting the clinical epidemiology; Risk of resistance development, in the presence/absence of host proteins.
Cytotoxicity	Including the bioactive agent with and without any carrier
Sterilization	Degradation/Stability of the carrier (and bioactive agent) upon sterilization

1- "Recommendations for design and conduct of preclinical in vivo studies of orthopedic device-related infection" T Fintan Moriarty et al, J of Orthopedic Research, **37**, Issue 2, 271-287, 2019 - https://onlinelibrary.wiley.com/doi/full/10.1002/jor.24230
2 - M Cloutier etal, AVS, Biointerphases **9**, 029013 (2014)
3 – Professor N hickok at FDS Anti-infection orthopedic implant workshop - http://fda.yorkcast.com/webcast/Play/8cd0cdbe08ea4b0088fe139199e733181d

Bacterium

Top bacteria

1. MRSA
2. MSSA
3. E.coli

Other Bacteria to consider

1. E.coli (11229 & 25922)
2. K. pneumonia (13883)
3. P. aeruginosa (15442 & 27853)
4. P. mirabilis (4675)
5. S. marcescens (14756)
6. S. aureus (6538 & 29213)
7. S. epidermidis (12228)
8. S. pyogenes (19615)
9. E. faecalis (29212)
10. E. faecium (19434)
11. C. acnes (6919)
12. B. fragilis (25285)
13. S. saprophyticus (15305)
14. M. luteus (7468)
15. C. albicans (10231)
16. C. tropicalis (75)
17. C. difficile (700057)

MRSA – Methicillin-resistance Staphylococcus aureus

MSSA - Methicillin-sensitive Staphylococcus aureus

E. coli – Escherichia coli

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FDA Orthopedic Device Infection Workshop – Nov 2020

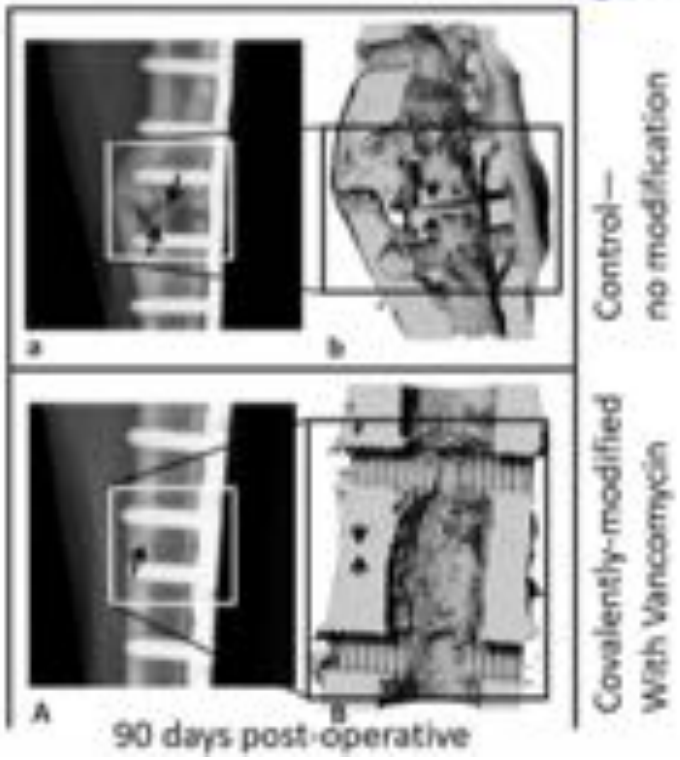
How much reduction in CFU is necessary?

Jefferson

Rule of thumb: $\geq 10^3$ CFU/ml

But:

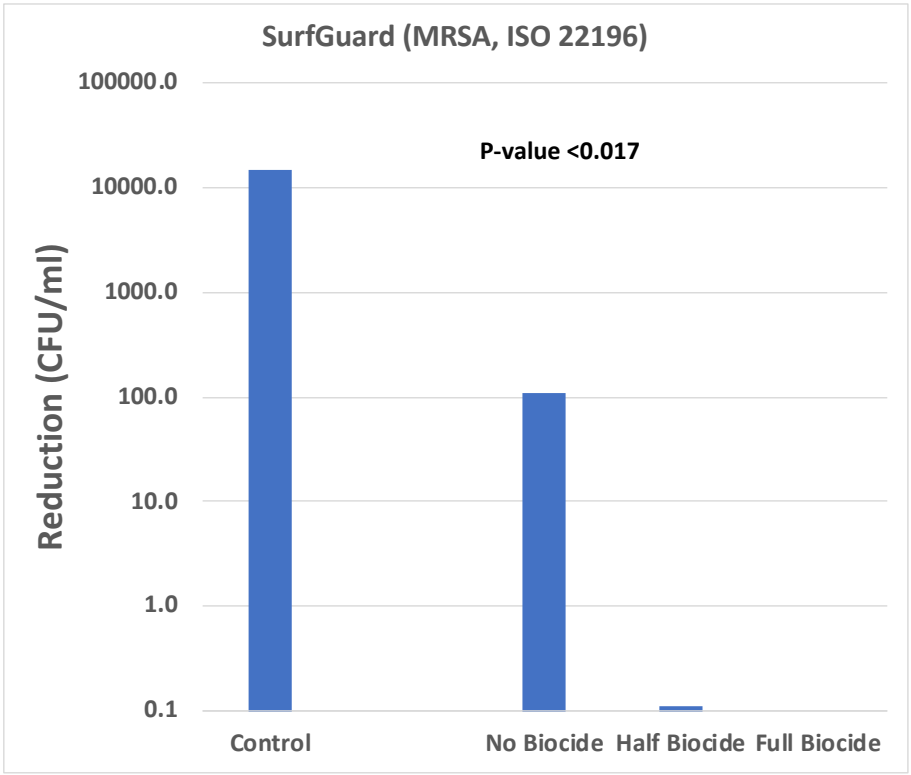
Our modified surfaces gave 10^1-10^2 CFU/ml reduction (*in vitro*) which was sufficient to prevent colonization in vivo



Professor N Hickok of Jefferson at the FDA Workshop http://fda.yorkcast.com/webcast/Play/8cd0cdbe08ea4b0088fe139199e733181d

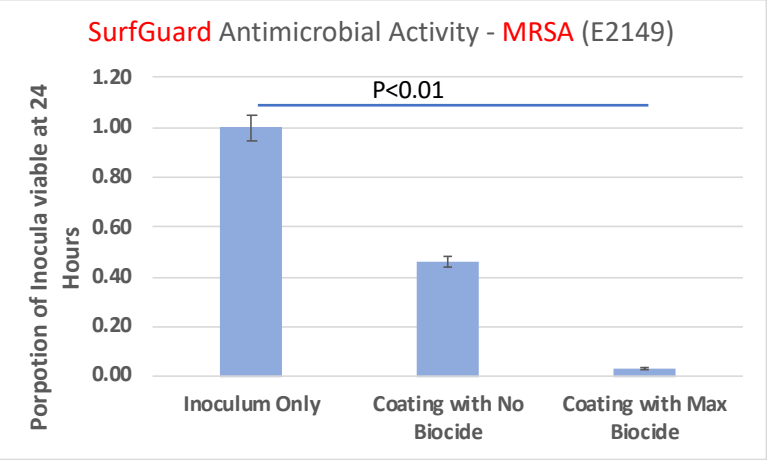
CFU= Colony Forming Unit

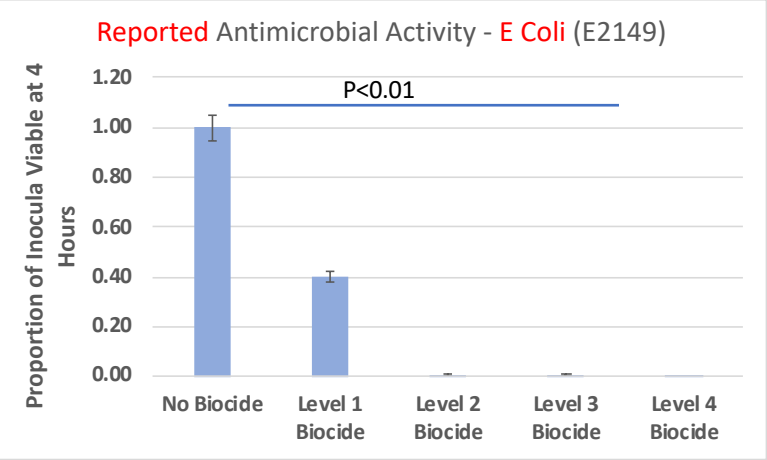
Antimicrobial Testing Results – ISO 22196



Antimicrobial Testing Results

- Range of 10^1 to 10^3 reduction on MRSA and E. Coli
  - Meets level reported by Prof Hickok at FDA workshop (Nov 2020)
  - Film optimization expected to improve reduction





Prof N Hickok (Jefferson U) - in vitro 10^1 to 10^2 reduction → prevents in vivo colonization (FDA workshop 13/11/ 2020)

In vitro 3 samples, multiple replication, ASTM E2149 Standard Test for Determining the Antimicrobial Activity Under Dynamic Contact Conditions
E.coli results: M Cloutier etal, AVS, Biointerphases **9**, 029013 (2014)

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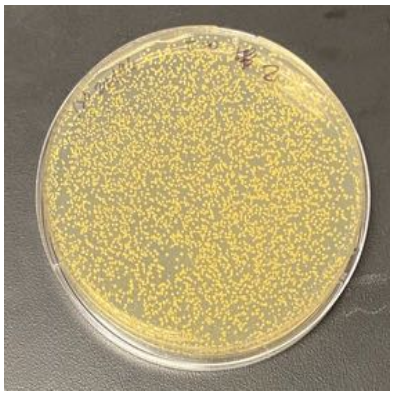
Antimicrobial Testing Results – ISO 22196

- 10^4 reduction (99.99% efficacy) on MRSA after 24 hours
  - Exceeds level reported by Prof Hickok at FDA workshop (Nov 2020)

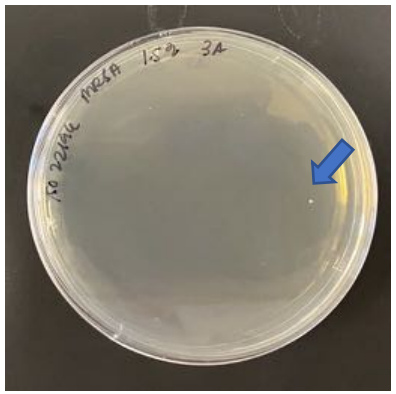


Control

- *S aureus* methicillin-resistant (MRSA) ATCC 33591
- Triplicate samples
- After 24 Hours

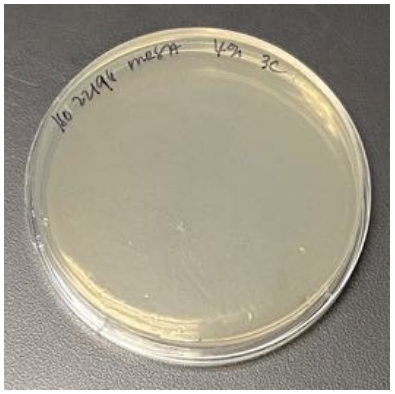
Diamond Film only

- Slight improvement
- Due to High lubricity



With Half Biocide

- **4 folds reduction**
- 99.99% efficacy
- One colony

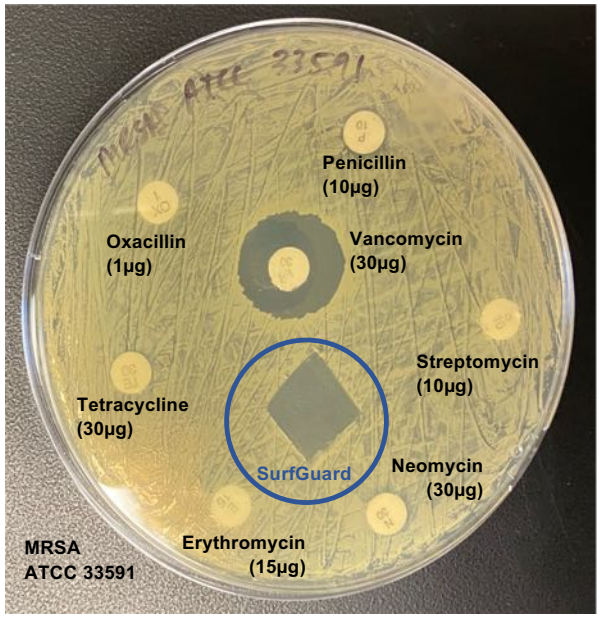


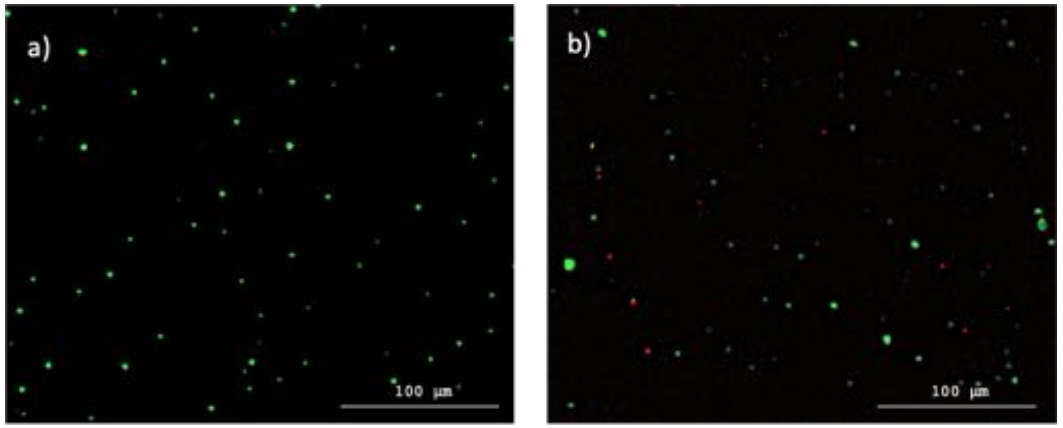
With Max Biocide

- **4 folds reduction**
- 99.99% efficacy
- No trace

International Organization for Standardization22196 . (2016). *Measurement of antibacterial activity on plastics and other non-porous surfaces* (ISO/DIS Standard No. 22196). Retrieved from https://www.iso.org/standard/54431.html

Kirby-Bauer Diffusion and Cell Viability testing Proof





No Diffusion on SurfGuard samples in K-B disk test on MRSA on Mueller-Hinton agar (+7 others)

LIVE/DEAD cell viability assay of MRSA (4 hrs.) on SurfGuard without (a) and with (b) Biocide – showing substantial reduction

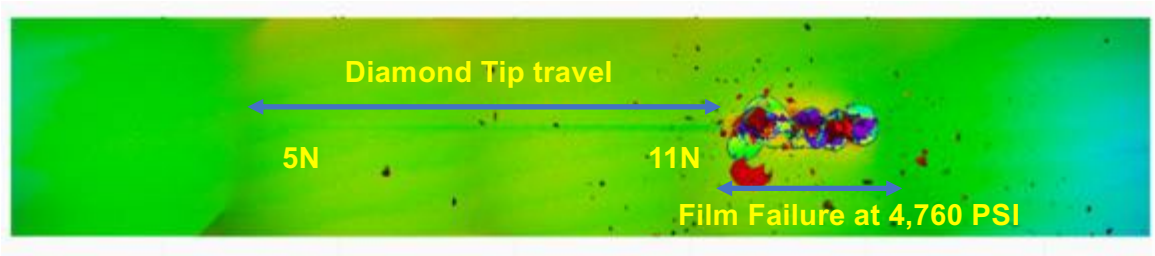
The live and dead cells exhibited green and red fluorescence, respectively.

Improved Wear rate Test

- Large (**~15x**) margin on joint contact pressure

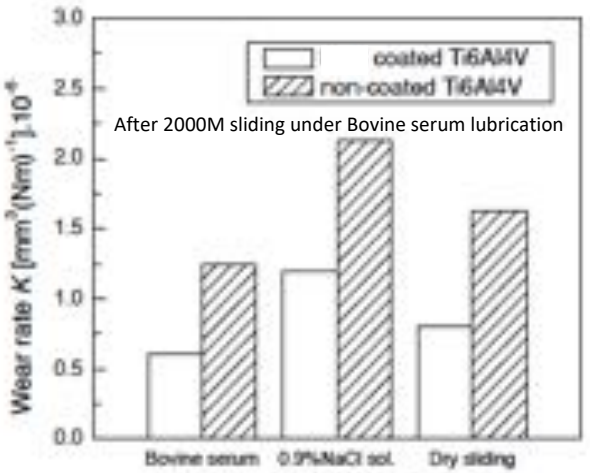
Part	Max Contact Pressure (PSI)	Ratio to Knee Joint
One Knee Joint only	320	1
Typical bone strength*	2611	~ 8x
SurfGurad™ critical load	4,760	~ 15x

- Lower wear rate: **2.5X** lower Coefficient of Friction



- No particulate or debris during multiple scratches

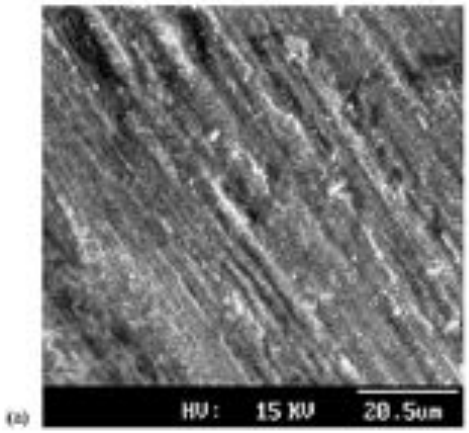
2x wear rate improvements



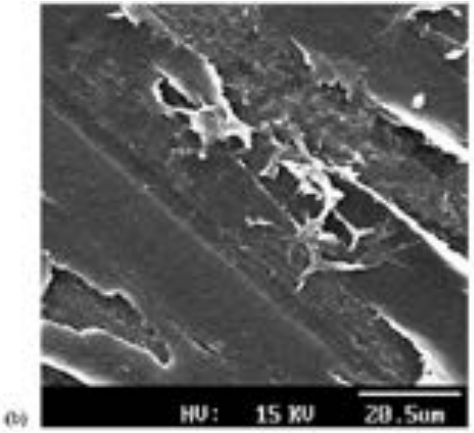
* SW Jain etal, Applied Surface Science 236 (2004) 285-291

Improved Wear Rate with **SurfGuard**

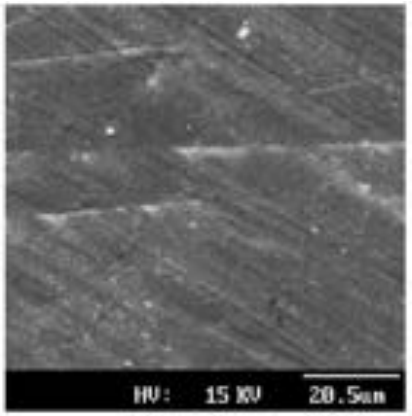
- **Improved wear rate depends on hardness, lubricity and formation of minimal debris**
- **Ti or CoCr alloys or UHMWPE surfaces after some use generate scratches and large debris respectably → increase wear**
- **SurfGuard shows no scratching or debris formation after similar use**



Bare Ti6Al4V - Rough Scratched Surface



UHMWPE - Large debris



SurfGuard - Minimal debris

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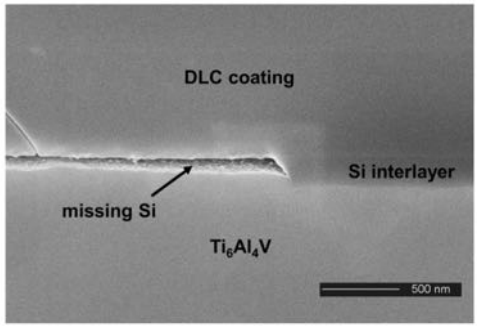
Crevice Corrosion

- Si highly vulnerable to corrosion in confined / crevice conditions
- High pitting corrosion susceptibility found in crevice due to local alkalization within a confined cathodic area.

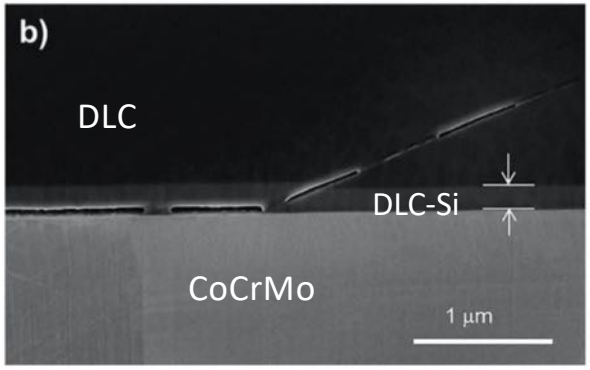
Crevice corrosion related attack appears where a Si interlayer has uniformly dissolved away



Silicon Corrosion in Neutral Media: The Influence of Confined Geometries and Crevice Corrosion in Simulated Physiological Solutions
Journal of The Electrochemical Society, 166 (6) C125-C133 (2019)

Corrosion Fatigue

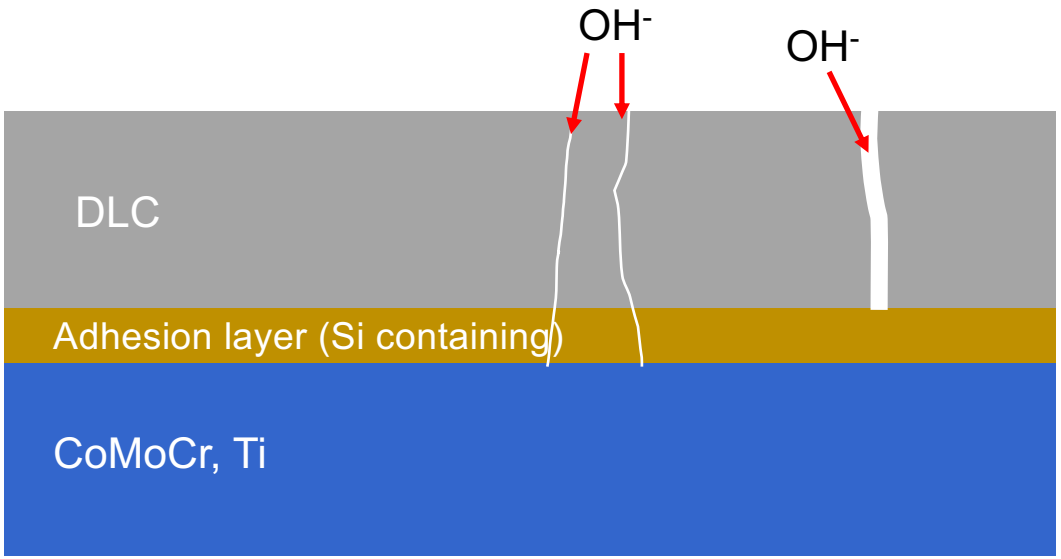
- Corrosion fatigue at buried interface of a Si-based adhesion-promoting interlayer in articulating implants on a CoCrMo biomedical alloy
  - DLC / DLC-Si / CoCrMo system
  - Reciprocal loading in body-like corrosive fluid
  - Under dynamic loading condition



Corrosion fatigue in DLC-coated articulating implants: an accelerated methodology to predict realistic interface lifetime
SCIENCE AND TECHNOLOGY OF ADVANCED MATERIALS 2019, VOL. 20, NO. 1, 173–186

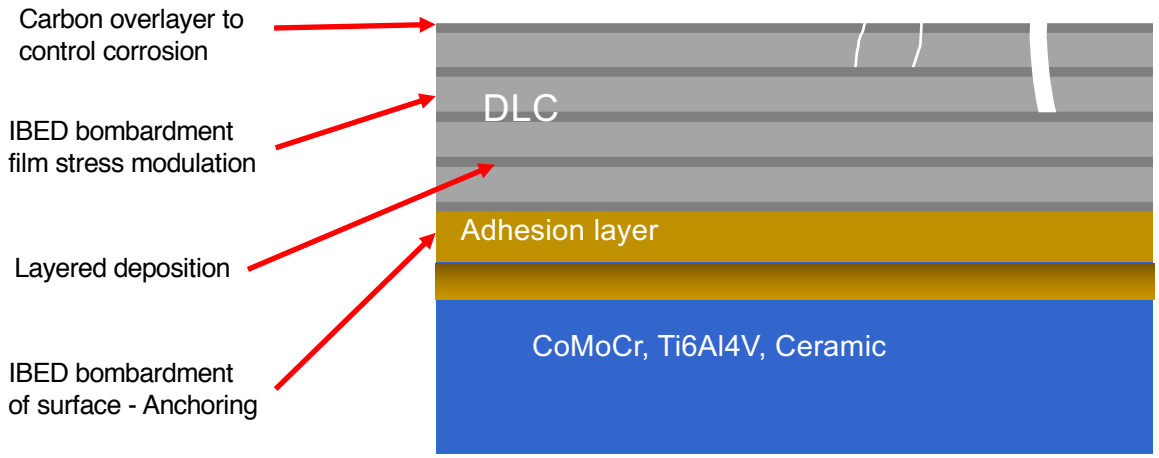
Possible Root Causes

- Adhesion layer (Si containing) corrosion in alkaline
- Film cracking – substrate surface defect propagate through
- Film delamination – high film stress
- Pin holes in film – film quality
- Coating adhesion



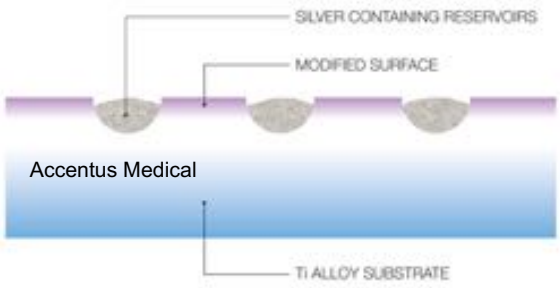
Possible Solutions

- Film adhesion / cracking
  - IBED bombardment of substrate interface to smooth/planarize surface
- Film delamination – lower film stress
  - IBED control of DLC layer to modulate film stress
- Pin holes in film – Layered deposition to stop crack/pinhole propagation
  - Deposition turn On/Off
- Don't use Si in coating
- Adhesion layer – carbides



Comparison of Agluna® and SurfGurad™

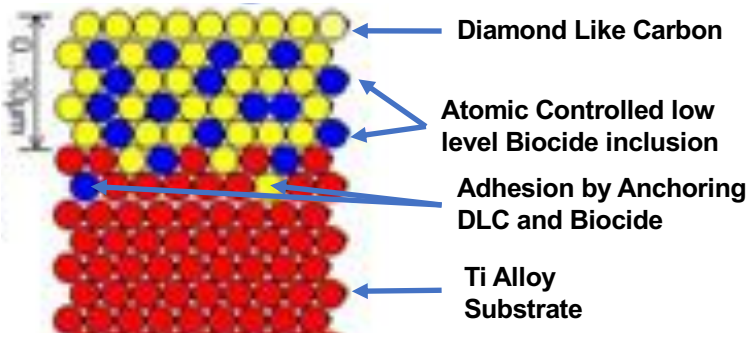
AGLUNA Technology



- Requires multiple step chemistry (metal specific, Plastics?)
- Silver Reservoirs and surface silver may lead to excess local cytotoxicity and staining
- High elution rate as 100% coating

http://www.accentus-medical.com/products-agluna.asp

SurfGuard Nano-Technology



- Single step applicable to all materials (Ag, I etc. possible)
- Very controlled biocide inclusion throughout the layer
- Low elution rate < few atomic %

Competitive Comparison

Body Part	Prosthetic	Film and Coatings	Antimicrobial (and antiviral)	Biocide Elution	Wear Rate and lubricious	Corrosion resistance	Osseointegration
Knee	Ti Alloy CrCo Zi Alloy	Polyethylene Plastic	No	NA	>Metal alloy and lubricious	Yes	No
		Ceramic Composites	No	NA	>Metal alloy	Brittle → corrosion	Possible
		Pyro Carbon	No	NA	Wear rate	Yes	?
Hip	Ti6Al4V	Plasma Sprayed Ti	No	NA	~ Metal alloy	Forms Oxide	Possible
		Hydroxyapatite	Ag inclusion	Short term	No	No	Yes
Competitors	Metal alloy	Agluna, Mutar	100% Ag Surface	High	~bare metal	No	No
SURFION	Metal or Plastic or ceramic	**SurfGurad**™	2.5x (Atomic % Throughout)	Minimal	2x (Lubricious Surface)	Contiguous film	Possible

Thank you

babak@surf-ion.com