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

NCCVAS Junction Tech UG

Babak Adibi - December 2022
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)

- **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

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

- Based on 2.5 Million Implants in US
- Skurtz et al J of Arthroplasty, 27, 8, Supp, 61-65, E1
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5110396/
- https://www.drugwatch.com/hip-replacement/surgery/
- https://www.hss.edu/conditions_revision-total-hip-replacement-overview.asp
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1888402/
Infection Progression Post Surgery

A. Time of Surgery
B. Instrumentations – Forced One time use
C. Biocide Attack – Minutes
D. Nano-Biocide layer formation – Hours/Day
E. Biocide colonies – Days/Weeks

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,
lubriicious instrumentation and
ease of cleaning

A. Time of Surgery:
Biocide defused Balloon
inserted or antibiotic injections

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

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

Surf-Ion Proprietary Information
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

Silver/DLC Bombardment
DLC/Silver Deposition
Silver Atoms
DLC Molecules
Ti6Al4V Prosthetics
## Anti-infectious In Vitro testing requirements

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

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/8cd0cde08ea4b0088fe139199e733181d](http://fda.yorkcast.com/webcast/Play/8cd0cde08ea4b0088fe139199e733181d)
# Bacterium

<table>
<thead>
<tr>
<th>Top bacteria</th>
<th>Other Bacteria to consider</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MRSA</td>
<td>9. E. faecalis (29212)</td>
</tr>
<tr>
<td>2. MSSA</td>
<td>10. E. faecium (19434)</td>
</tr>
<tr>
<td>3. E. coli</td>
<td>11. C. acnes (6919)</td>
</tr>
<tr>
<td></td>
<td>12. B. fragilis (25285)</td>
</tr>
<tr>
<td></td>
<td>13. S. saprophyticus (15305)</td>
</tr>
<tr>
<td></td>
<td>14. M. luteus (7468)</td>
</tr>
<tr>
<td></td>
<td>15. C. albicans (10231)</td>
</tr>
<tr>
<td></td>
<td>16. C. tropicalis (75)</td>
</tr>
<tr>
<td></td>
<td>17. C. difficile (700057)</td>
</tr>
</tbody>
</table>

|                       |                                               |
|                       | 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)                        |

MRSA – Methicillin-resistance Staphylococcus aureus
MSSA - Methicillin-sensitive Staphylococcus aureus
E. coli – Escherichia coli
Rule of thumb: $\geq 10^3$ CFU/ml

But:
Our modified surfaces gave $10^1$-$10^3$ CFU/ml reduction (in vitro) which was sufficient to prevent colonization in vivo
Antimicrobial Testing Results – ISO 22196

![Bar graph showing reduction in CFU/ml of SurfGuard (MRSA, ISO 22196)]

- Control
- No Biocide
- Half Biocide
- Full Biocide

P-value < 0.017

Surf-Ion Proprietary Information
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)
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

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
- Lower wear rate: 2.5X lower Coefficient of Friction
- No particulate or debris during multiple scratches

<table>
<thead>
<tr>
<th>Part</th>
<th>Max Contact Pressure (PSI)</th>
<th>Ratio to Knee Joint</th>
</tr>
</thead>
<tbody>
<tr>
<td>One Knee Joint only</td>
<td>320</td>
<td>1</td>
</tr>
<tr>
<td>Typical bone strength*</td>
<td>2611</td>
<td>~ 8x</td>
</tr>
<tr>
<td>SurfGurad™ critical load</td>
<td>4,760</td>
<td>~ 15x</td>
</tr>
</tbody>
</table>

2x wear rate improvements

After 2000M sliding under Bovine serum lubrication

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 respectively → increase wear
- SurfGuard shows no scratching or debris formation after similar use
**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.

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**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

Silicon Corrosion in Neutral Media: The Influence of Confined Geometries and Crevice Corrosion in Simulated Physiological Solutions

Corrosion in Simulated Physiological Solutions
Silicon Corrosion in Neutral Media: The Influence of Confined Geometries and Crevice Corrosion in Simulated Physiological Solutions
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

Carbon overlayer to control corrosion
IBED bombardment film stress modulation
Layered deposition
IBED bombardment of surface - Anchoring

DLC
Adhesion layer
CoMoCr, Ti6Al4V, Ceramic
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

**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

<table>
<thead>
<tr>
<th>Body Part</th>
<th>Prosthetic</th>
<th>Film and Coatings</th>
<th>Antimicrobial (and antiviral)</th>
<th>Biocide Elution</th>
<th>Wear Rate and lubricious</th>
<th>Corrosion resistance</th>
<th>Osseointegration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee</td>
<td>Ti Alloy CrCo Zi Alloy</td>
<td>Polyethylene Plastic</td>
<td>No</td>
<td>NA</td>
<td>&gt;Metal alloy and lubricious</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Ceramic Composites</td>
<td></td>
<td>No</td>
<td>NA</td>
<td>&gt;Metal alloy</td>
<td>Brittle → corrosion</td>
<td>Possible</td>
</tr>
<tr>
<td></td>
<td>Pyro Carbon</td>
<td></td>
<td>No</td>
<td>NA</td>
<td>Wear rate</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td>Hip</td>
<td>Ti6Al4V</td>
<td>Plasma Sprayed Ti</td>
<td>No</td>
<td>NA</td>
<td>~ Metal alloy</td>
<td>Forms Oxide</td>
<td>Possible</td>
</tr>
<tr>
<td></td>
<td>Hydroxyapatite</td>
<td></td>
<td>Ag inclusion</td>
<td>Short term</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Competitors</td>
<td>Metal alloy</td>
<td>Agluna, Mutar</td>
<td>100% Ag Surface</td>
<td>High</td>
<td>~bare metal</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

| SurfGurad™ | 2.5x (Atomic % Throughout) | Minimal | 2x (Lubricious Surface) | Contiguous film | Possible |

Surf-Ion Proprietary Information
Thank you

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