Metal Implants and Immune Response: Pre- and Post-Market Methods for Evaluating Corrosion and Wear Debris from Medical Devices Containing Metal

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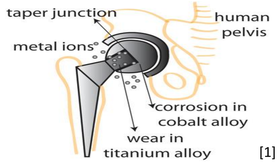
Introduction



[1]

Background

- Recent post-market signals for metal implants suggest that subsets of patients develop unexpected or heightened biological responses from prolonged metal exposure.
- There is a variation and disagreement in recognized standards for the implantation, recovery, and assessment of implanted medical devices.

Objective

- The goal of this project is to work with internal and external partners to identify gaps in current standards for assessment of corrosion, implant wear, associated biological response in patients, as well as assessment of the consistency with which the methods are applied.

Methods

Review Guidance Documents, Standards, and Scholarly Articles

- Literature review assessing the availability and usefulness of methods used for analyzing retrieved implants were conducted (methods to evaluate tribocorrosion, in vivo imaging, metal levels in body fluids and tissues, tissue retrieval and histological assessments).
- We conducted cross-institutional training to apply best-targeted literature search practices.

OPEQ interviews

- Reached out to biocompatibility focal points program to identify subject matter experts (SME) from each office of health technology (OHT).
- Interviewed representative subject matter expert from each OHT.

Deliverables

PUBLICATIONS

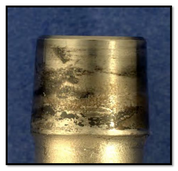
Publishing (White Paper)

- Paper presenting FDA's views on currently available scientific information related to immunological responses to metal-containing implants.
  - Gaps in frequently used standards for evaluating wear and corrosion in medical implants.
  - Opportunities for further research.

Wear Project (Future Work)

- Wear testing in commonly used implant materials like Titanium and Stainless Steel.
  - Evaluating metal release and third body wear in an *ex-vivo* condition.
  - Address gaps identified.

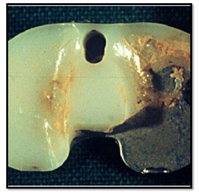
Standards and Identified Gaps


Corrosion in dental Implants [2]

Frequently Used Corrosion Standards Corrosion in medical implants is categorized in various ways which includes: General corrosion (ASTM F3306), Pitting corrosion (ASTM F2129), Crevice corrosion (ASTM F746), Fretting corrosion (ASTM F1875), and Galvanic corrosion (ASTM 3044) [4,5].

Gaps in Standards

- ASTM F746 was initially developed for screening the properties of metallic materials, but the scope of the standard does not include the evaluation of device design on crevice corrosion potential.
- Standards such as ASTM F1875 suggests two methods to evaluate fretting corrosion. However, the relative contribution of mechanical and electrochemical processes to the total corrosion have not been established.
- Moreover, electrochemical methods often determine wear rate based on Faraday's law however, no acceptance criteria for fretting corrosion currents are included in the electrochemical test description.


Wear in Knee Implants [3]

Wear Standards Frequently Used

- Wear testing on metal implants is generally performed on a finished medical device or one that has been manufactured and processed in the same way as that which would be used clinically. The performance and material degradation due to wear is device-specific.
  - Wear testing of joint replacement prostheses are primarily described in ISO 14243, ISO 14242, and ISO 22622. addressing total knee, hip, and ankle joint replacement prostheses, respectively.
  - Wear testing of spinal implants is performed with particular focus on impingement evaluation. The positioning and angles used in ISO 18192-1 and 18192-2 replicate that found in a representative total intervertebral spinal disc prosthetic physiological environment [6].

Gaps in Standards

- *No specific standard to evaluate wear in dental devices:* Dental devices are covered by a variety of methods to evaluate surface changes as described in ISO 10271:2020 like static immersion, electrochemical, and crevice corrosion testing. Although, the language does not mention wear, the depicted methods capture this aspect of material degradation in non-loaded conditions.
- *Imaging and visualization of specimen after wear test is not standardized*: To capture both signs of wear and corrosion on the surface of medical devices, imaging is often done without magnification. Due to this change in magnification, intricate details on the surface could get neglected and clear evaluation might not be possible.

Perspective of Regulatory Scientists

1. We created a series of questions covering:
   - General questions for metal Implanted device
   - Clinical and pre-clinical practice of implantation
   - Imaging of metal implants (various modalities)
   - Physical and chemical analyses of metal in tissue
   - Tissue sampling in vivo/ex vivo
   - Assessment of wear and corrosion of metal implants
2. We vetted these questions through 32 researchers across:
   - Materials Science and Engineering
   - Regulatory Science
   - Health Science
   - Biomedical Engineering
   - Pharmacology
   - Biology
   - Microbiology
3. We reached out to Focal Point Programs to identify subject matter experts across all Offices of Health Technology (OHT):
   - Focal Point Programs work to provide consistency in review of medical devices across all OHTs
4. We interviewed individuals representing each OHT and Office of Clinical Evidence and Analysis (OCEA):
   - Ophthalmic, dental, ear-nose-throat devices
   - Cardiovascular devices
   - Reproductive, gastro-renal, urological devices
   - Surgical and infection control devices
   - Neurological and physical medicine devices
   - Orthopedic devices
   - In vitro diagnostics and radiological devices
5. We collected feedback on the need for standardized approaches to reviewing medical devices containing metals:
   - 27 SMEs identified
   - 1 hour per interview
   - Email follow-up with all SMEs

Initial Observations:

Standardization of methods may not be practical, such as investigating a fractured versus thrombosed device. It may be helpful to first identify failure modes of interest and then we can draft a standardized set of properties for each mode.

For dental restorative materials that involve dissimilar metals, there is no acceptance criteria for corrosion.

In the absence of standardized methods, interactive conversations between industry and regulators are essential for robust experimental design.

Animal models typically capture healthy state, though medical devices may be indicated for unhealthy patient populations.

There can be a lot of variation in review practices across the center.

We want your feedback!

Comments and suggestions can be sent to me at my email (Sherrill.Blitzer@fda.hhs.gov) *with a Subject line* 'Clinically relevant wear poster'.

References

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