

# What It Means To Go 'Off-Label'

Tobias Gilk - Sept 27, 2022

**GRC** 2022 Dubai Advanced MRI Safety Seminar

Going 'Off-Label'

# Outline

## What It Means To Go 'Off-Label'

- Intro
- How Patients Are Harmed In MRI
- 'Off-Label' ≠ Automatically Unsafe
- It's About The Harm
- Tools For Quantifying Risk & Categorizing Devices
- Q & A

# How Are Patients Harmed In MRI?

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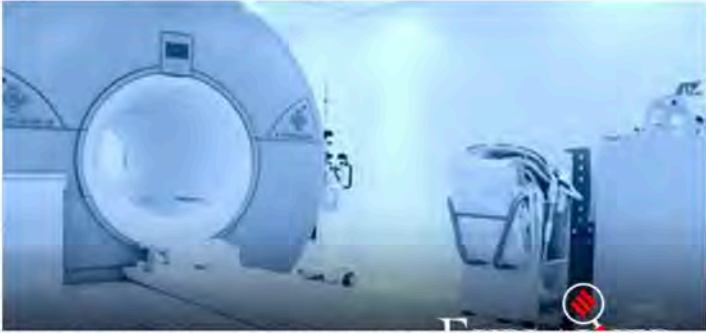
[Home](#) / [Explained](#) / Explained: How an MRI machine killed a man in Mumbai

## Explained: How an MRI machine killed a man in Mumbai

Bombay High Court has directed BMC to pay interim compensation of Rs 10 lakh to the family Rajesh Maru, who was killed after he was sucked into an MRI machine at BYL Nair Hospital in January 2018.




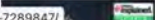
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By: **Explained Desk** | Mumbai |  
Updated: September 19, 2019 9:56:20 pm



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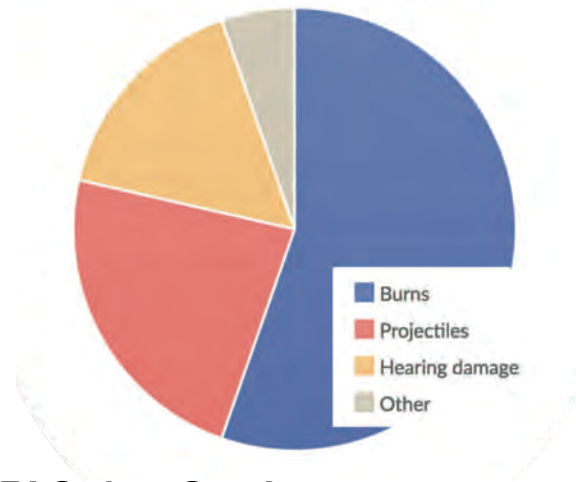
### MORE EXPLAINED

-  Why US lifted the pause on Johnson and Johnson's single-shot Covid-19 vaccine
-  What Frances McDormand's Oscars triumph reveals – and conceals – about older women characters in Hollywood
-  How Covid-anxiety is affecting cricketers in the IPL
-  How Ravindra Jadeja

[/explained/explained-what-frances-mcdormands-oscars-triumph-reveals-and-conceals-about-older-women-characters-in-hollywood-7289847/](#)

# How Are Patients Harmed In MRI?

**95%**  
OF REPORTED  
INJURIES WE ANALYSED  
WERE RELATED TO BURNS,  
PROJECTILES OR  
HEARING DAMAGE



However...

Internal (Implant-Related) Injuries Are NOT Well Quantified.

# How Are Patients Harmed In MRI?

## MAUDE Adverse Event Report: MRI

[FDA Home](#) [Medical Devices](#) [Databases](#)



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### MRI

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**Device Problem** Improper or Incorrect Procedure or Method (2017)

**Patient Problems** Death (1802); Hemorrhage, Subarachnoid (1893)

**Event Date** 08/12/2016

**Event Type** Death

#### Event Description

My father had an mri of the spine ordered at (b)(6) center. He has a history of a craniotomy for aneurysm clipping in 1982, and should not have an mri due to the risk of migration of clips and possible bleeding. Md well aware of his history, and ordered mri anyway. During the mri, my father became unresponsive and was posturing. A f/u ct scan of the brain showed a massive subarachnoid hemorrhage. He passed away about 15 hours later. After the mri and hemorrhage event, md came to speak to my mother, and informed her that they had made a mistake, and that the mri should never have been ordered, and likely caused the massive brain hemorrhage. I am concerned that they ordered this test, being well aware of the fact that my father had aneurysm clips in his brain, as this was documented in his admitting h&p, by the very md that ordered the mri. Please investigate.

[Search Alerts/Recalls](#)

# How Are Patients Harmed In MRI?

## A woman dies after a resonance 'blows' her morphine pump

The patient had the device for the administration of this opiate four years before because of her back pains





# How Are Patients Harmed In MRI?

- Implant & Device Adverse Events Can Be Some Of The Most Dangerous!
- While Very Rare, The Poor Quantification (And Reluctance To Discuss Them) Leads Us To Mis-Estimate Risk.

# How Are Patients Harmed In MRI?

“Cowboys” and “Ghosts”



# **'Off-Label' ≠ Automatically Unsafe**

# 'Off-Label' ≠ Automatically Unsafe

## MR Unsafe

Known to pose hazards in all MRI environments



MR Unsafe - an item that is known to pose hazards in all MRI environments. MR Unsafe items include magnetic items such as a pair of ferromagnetic scissors.

# 'Off-Label' ≠ Automatically Unsafe

## MR Unsafe

- Labeled “MR Unsafe” Is An Affirmative Condition...  
“Known to pose (unacceptable) hazards in MR environment”
- If You Only *Presume* The Hazard, That Doesn't Make A Device “Unsafe Equivalent”

# 'Off-Label' ≠ Automatically Unsafe

- Outside of MR Conditional Conditions or “off-label” means device manufacturer does not promise safety.

# 'Off-Label' ≠ Automatically Unsafe

- Sites may elect to presume “off-label” is unsafe (unless / until further information is developed), but this is operational.

# 'Off-Label' ≠ Automatically Unsafe

- Presumption is based on ignorance, not informed risk-assessment.





# It's About Harm

# It's About Harm

- If you can't identify the specific harms at risk, you can't mitigate them.

# It's About Harm

## Static Magnetic Field Harms

- Twisting (B0)
- Pulling (SFG)
- Device Functional Interference

# It's About Harm

## Time-Varying Gradient Harms

- Neuromuscular Stimulation
- Vibration
- “False Feedback” (for active, sensing devices)
- Heating (often not clinically significant)

# It's About Harm

## Radio Frequency (RF) Magnetic Field Harms

- Diffuse Thermal Loading (typically managed by MRI scanner)
- Focal Heating

# Tools For Quantifying Risk & Categorizing Devices

# **Tools For Quantifying Risk & Categorizing Devices**

## **Working From MR Conditional Labeling**

If you're going 'off-label' for...

# Tools For Quantifying Risk & Categorizing Devices

## Working From MR Conditional Labeling

If you're going 'off-label' for...

Field Strength: For Torque: All lesser values included

For RF Heating: May be introducing greater risks



# Tools For Quantifying Risk & Categorizing Devices

## Working From MR Conditional Labeling

If you're going 'off-label' for...

Spatial Gradient:      For Translation / Attraction: All lesser values included

# Tools For Quantifying Risk & Categorizing Devices

## Working From MR Conditional Labeling

If you're going 'off-label' for...

Time-Varying  
Gradient:

For Stimulation & Vibration: All lesser values included

# Tools For Quantifying Risk & Categorizing Devices

## Working From MR Conditional Labeling

If you're going 'off-label' for...

RF SAR / B1+:      For Heating: All lesser values included

# Tools For Quantifying Risk & Categorizing Devices

## Working From MR Conditional Labeling

If you're going 'off-label' for...

Patient Position: Changing position may change exposures & may significantly change risk profile.

# Tools For Quantifying Risk & Categorizing Devices

## Categorical Safety Statements

What Are Categorical Safety Statements?

- When An Entire Category Of Implants Have...
  - Similar shapes / sizes
  - Similar material composition

We can begin to identify safety profile by class / category.

# Tools For Quantifying Risk & Categorizing Devices

## Categorical Safety Statements

When Do Categories NOT Work?

- When Implants Within A Category Have...
  - Very different sizes / shapes
  - Different material composition

For example, coronary stents vs. femoral stents

# Tools For Quantifying Risk & Categorizing Devices

## Categorical Safety Statements

- Dr. Kanal Statements On Coronary Stents
- Dr. Sherlock Statements On
  - Coronary Stents
  - Annuloplasty Rings
  - Artificial Heart Valves

# Tools For Quantifying Risk & Categorizing Devices

## Categorical Safety Statements

**Guidelines for the Management of Patients with Coronary Artery Stents  
Referred for MRI Procedures**

Frank G. Shellock, Ph.D., FACR, FISMRM, FACC  
Adjunct Clinical Professor of Radiology and Medicine  
Keck School of Medicine, University of Southern California  
[www.MRIsafety.com](http://www.MRIsafety.com)



# Tools For Quantifying Risk & Categorizing Devices

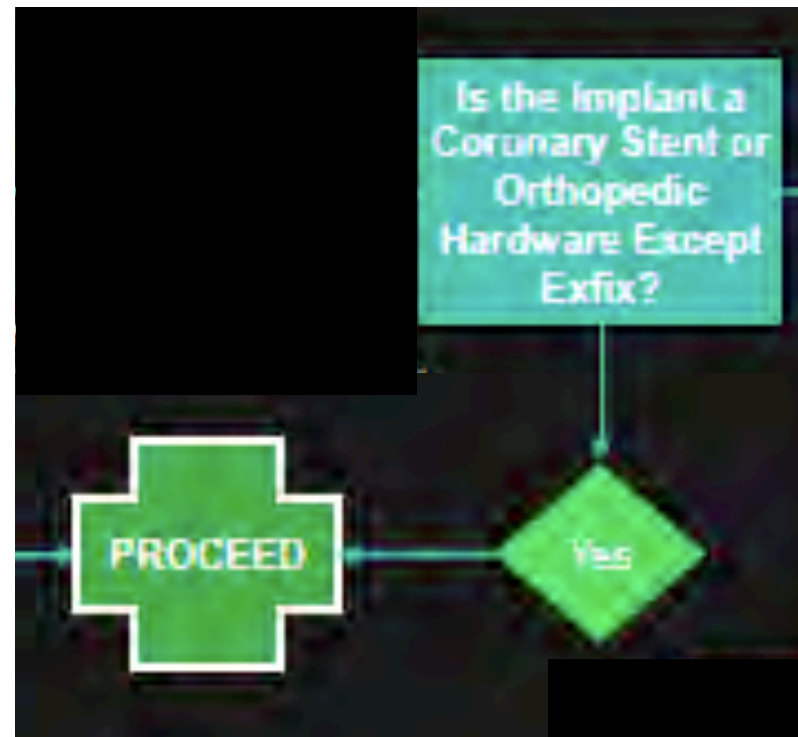
## Categorical Safety Statements

MRI labeling information exists for many coronary artery stents (3, 22). By following the pertinent MRI labeling information (i.e., presented in the Instructions for Use, Patient Identification Card, etc.), patients with coronary artery stents have safely undergone MRI examinations, including those performed at 1.5- and 3-Tesla. Importantly, there has never been an adverse event reported in association with performing MRI in patients with these particular implants.

# Tools For Quantifying Risk & Categorizing Devices

## Categorical Safety Statements

- I have worked with some radiologists who make site safety statements about passive orthopedic implants.
- Categorical safety statements are at the discretion / authority of the supervising physician (radiologist).



# Tools For Quantifying Risk & Categorizing Devices

## Exposure Analysis

- It *WILL* be exposed to static magnetic fields
  - Field Strength of Exposure (Torque)
  - Spatial Field Gradient of Exposure (Translation)
- To What Degree will it be exposed to Time-Varying Gradients?
- To What Degree will it be exposed to RF Magnetic Fields?

# Tools For Quantifying Risk & Categorizing Devices

## Exposure Analysis

### C. Heating

The radiofrequency (RF) and time-varying gradient fields (dB/dt) of the MR system can induce heating of the tissue adjacent to the medical device and/or heating of the medical device itself. This hazard should be addressed for all medical devices anticipated to enter the bore of the MR system.

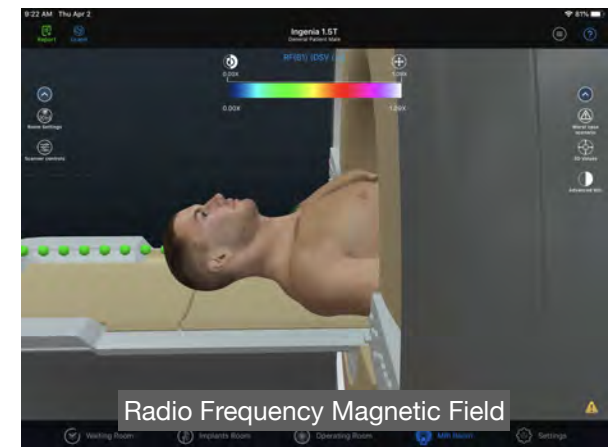
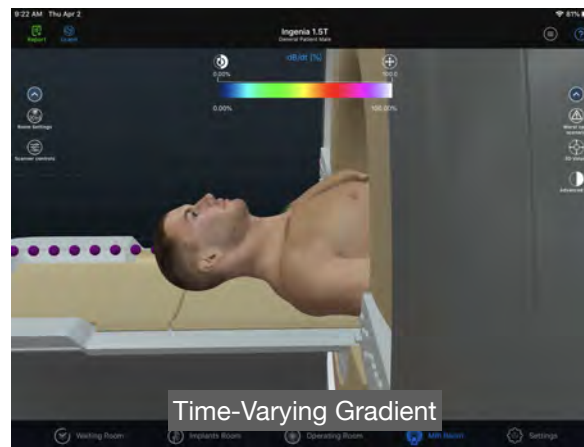
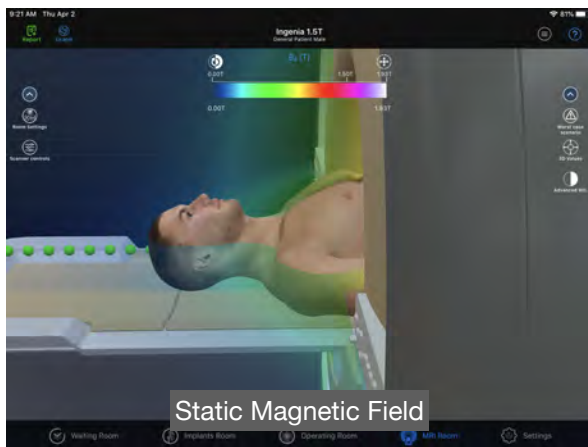
“Testing and Labeling Medical Devices for Safety in the Magnetic Resonance (MR) Environment”  
US FDA (2021)

# Tools For Quantifying Risk & Categorizing Devices

## Exposure Analysis

In other words...

- If it's wholly outside the bore, it will not be exposed to meaningful RF, nor meaningful time-varying gradient energies.



# Tools For Quantifying Risk & Categorizing Devices

## Materials Analysis - Static Magnetic Field

- These Are Some Nominally Non-Magnetic Materials
  - 316L Stainless Steel
  - Nitinol
  - Phynox
  - Elgiloy
  - Titanium (CP)

# Tools For Quantifying Risk & Categorizing Devices

## Materials Analysis - Time Varying Gradients & RF

- These Are Some Nominally Non-Electrically Conductive Materials
  - Silicone
  - PEEK
- Greater Risks From Insulated Electrical Conductors

# Tools For Quantifying Risk & Categorizing Devices

## Size Analysis

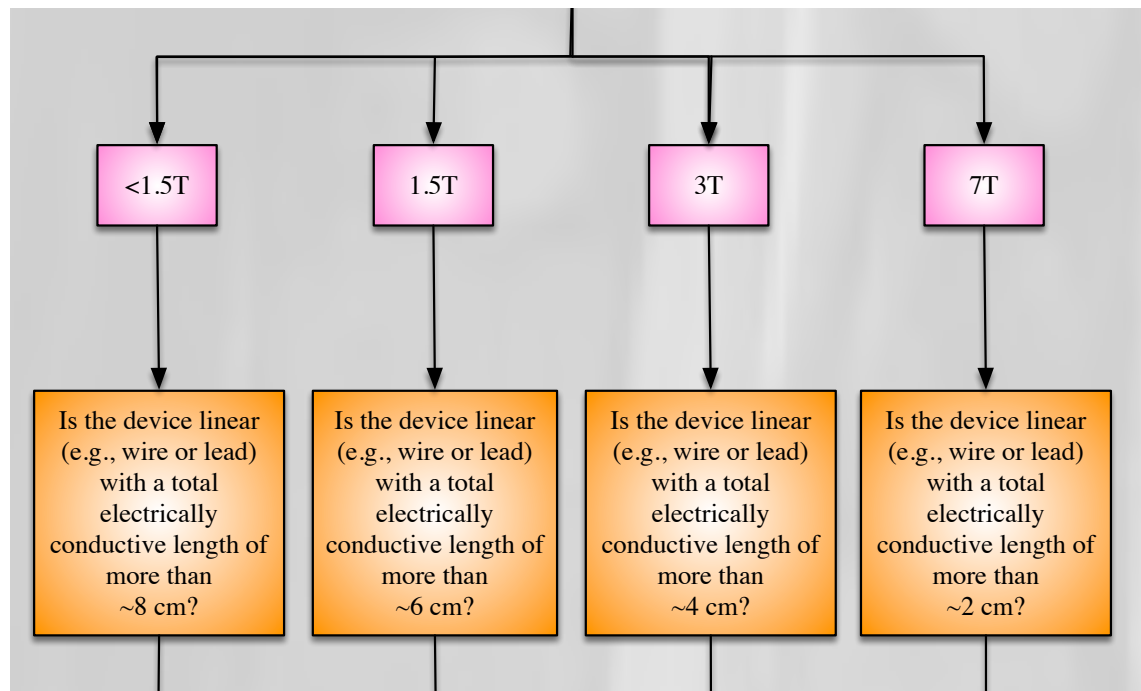
A passive implant with dimensions of less than 2 cm in all directions and at least 3 cm away from another passive implant does not need to be tested with respect to RF induced heating at 3.0 T or less, as it is expected to generate a temperature increase of less than 2 °C in Normal Operating Mode, over the course of 1 hour of exposure. This test exclusion is not valid (i)

**“Testing and Labeling Medical Devices for Safety in the Magnetic Resonance (MR) Environment”  
US FDA (2021)**



# Tools For Quantifying Risk & Categorizing Devices

## Size Analysis

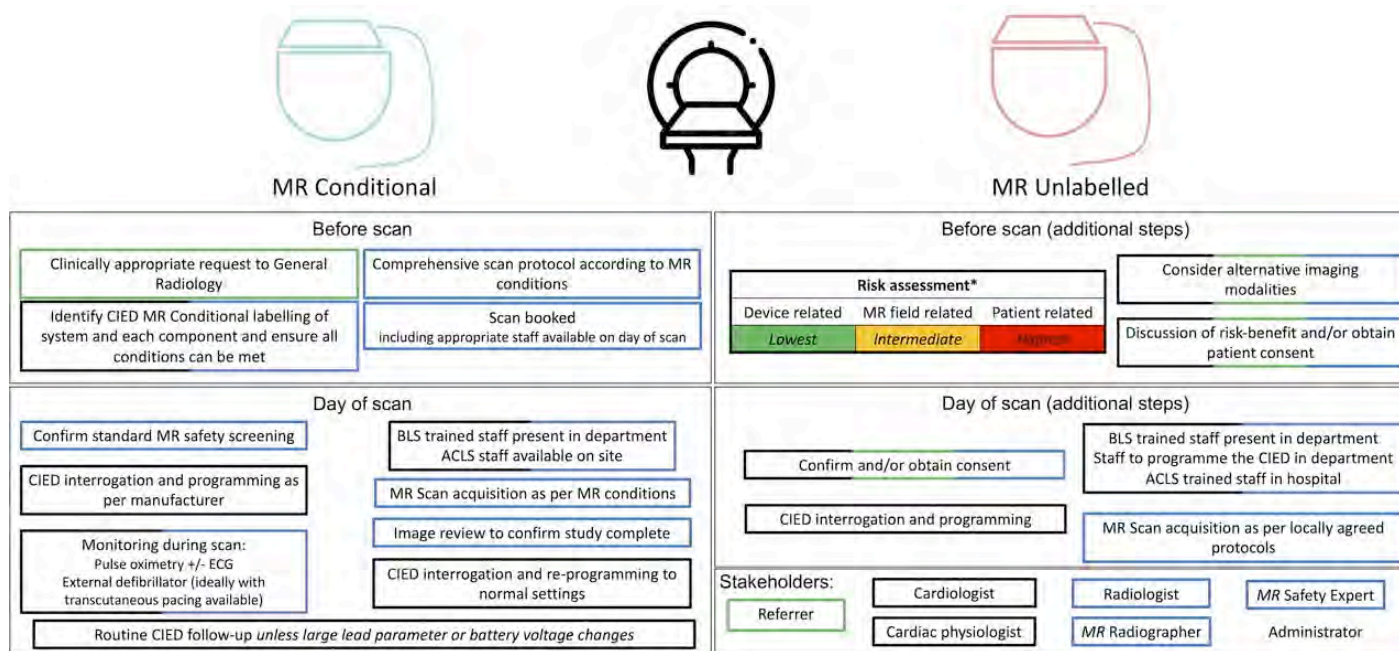


“MR Safety Implant Decision Tree Diagram v. 1.6”

Dr. Emanuel Kanal

# Tools For Quantifying Risk & Categorizing Devices

## Literature



Joint British Society consensus recommendations for magnetic resonance imaging for patients with cardiac implantable electronic devices  
<https://heart.bmj.com/content/early/2022/09/14/heartjnl-2022-320810>

**“I Can’t Go Off-Label”**

# **“I Can’t Go Off-Label”**

## **But You Already Do... All The Time.**

- GBCA Contrast Studies
  - Brain & Spine
  - Arterial / Vascular / Run-Off
  - Arthrogram
  - Breast
  - Pediatric Populations

# “I Can’t Go Off-Label” But You Already Do... All The Time.

- GBCA Contrast Studies

## *Off-Label Use of MRI Contrast Agents*

In the past, radiologists often used GBCM in an off-label fashion (e.g., off-label higher doses or off-label indications). By definition, such usage is not approved by the FDA. However, physicians have some latitude in off-label GBCM use as guided by clinical circumstances as long as they can justify such usage in individual cases.

[https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast\\_Media.pdf](https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf)

# **“I Can’t Go Off-Label”**

## **But You Already Do... All The Time.**

How did you decide to use contrast off-label?

- Reviewed literature?
- Consulted with peer experts?
- Consulted with certified MRI safety professionals?

# Going 'Off-Label' Can Be Best Practice

# Going 'Off-Label' Can Be Best Practice

- IV Valium & Status Epilepticus



# Clinical Decision-Making To Go 'Off-Label'

# Clinical Decision-Making To Go 'Off-Label'

- Risk v. Benefit

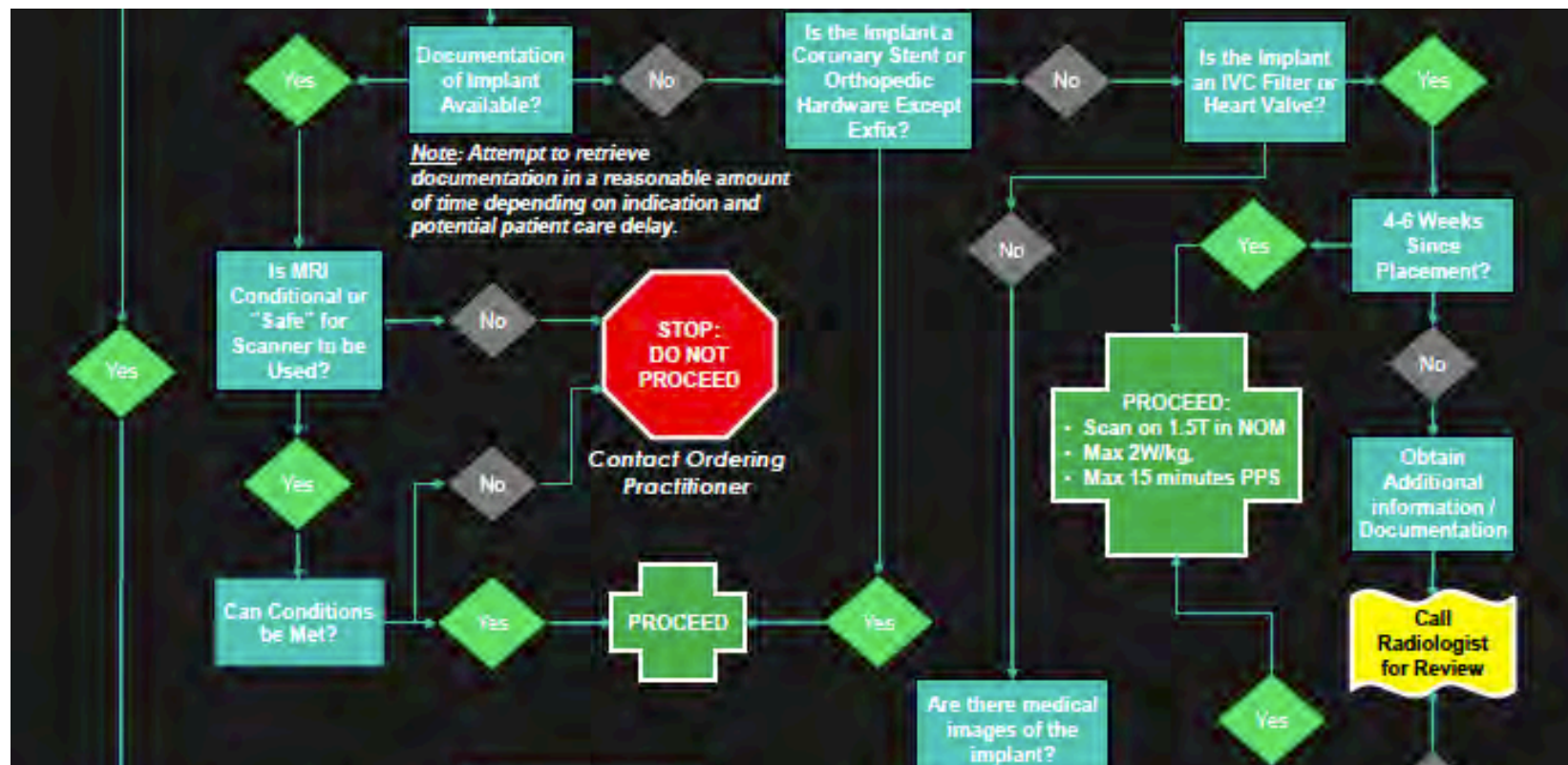
## Risk

- Can be informed / quantified by anyone

## Benefit

- To be determined by exam-supervising physician

# Clinical Decision-Making To Go 'Off-Label'



# Q&A

# Thank You

**Tobias Gilk, MRSO, MRSE**



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