Health informatics and AI, the road to Interoperability

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INFORMATION TECHNOLOGY STANDARDS

SC 42 – Artificial Intelligence

No Global Consensus on AI definition

- Different definition used by regulators, providers, standards organizations, developers
- International Medical Device Regulators Forum (IMDRF) working towards publishing glossary in Q2 2022
  - IMDRF started with 16 different definitions
  - EU proposed 6 different definitions
  - Eventually, IMDRF decide to not define AI at all

What is AI? FDA…

- **Artificial Intelligence** has been broadly defined as the science and engineering of making intelligent machines, especially intelligent computer programs (McCarthy, 2007). Artificial intelligence can use different techniques, including models based on statistical analysis of data, expert systems that primarily rely on if-then statements, and machine learning.

- **Machine Learning** is an artificial intelligence technique that can be used to design and train software algorithms to learn from and act on data. Software developers can use machine learning to create an algorithm that is 'locked' so that its function does not change, or 'adaptive' so its behavior can change over time based on new data.
  Some real-world examples of artificial intelligence and machine learning technologies include:
  - An imaging system that uses algorithms to give diagnostic information for skin cancer in patients.
  - A smart sensor device that estimates the probability of a heart attack.

NOTE: AI encompasses wide spectrum of software tech ranging from simpler "if -> then" statements, look up tables to Machine Learning to Deep Learning.

Medical devices based on "medical device data" and using ARTIFICIAL intelligence technology to achieve their intended use (i.e., medical use)

NMPA AI Definition

- **AI MD has a clear definition** from "AI Medical Device Registration Review Guideline"**(No. 8, 2022) on March 9,22**
- AI Medical Device[1] is the medical devices based on "**medical device data**" and using **artificial intelligence technology** to achieve their **medical purposes** (i.e, medical use)
- Medical device data: 1)**medical images**(X-Ray, CT, MRI, U/S, etc.); 2) **physiological signals,** e.g ECG, EEG; 3)IVD- **pathological images**, etc.); 4)data generated by non-MD with medical use, e.g. digital health product generated ECG data, etc.

NMPA AI Classification

- AI MD will be **Class II** or **Class III** (SaMD or medical device with AI SW component belongs to Class III);
- Classify as **CAD** (Computer-aided detection/diagnosis/triage) or **non-CAD** (e.g. process optimization, image quality/speed improvement, automatic measurement/segmentation, 3D reconstruction) **by clinical unities.**

NMPA AI Class III practice in China

Local AI players

- **30** of 31 **local players**[2] got NMPA AI SaMD clearance
- Smooth AI clearance with faster innovation as **NMPA requirement fully incorporated into local R&D process** including **Chinese population training data**, validation by Chinese physician and **clinical trial** data;

MNC

- **Only 1** MNC got NMPA Class III clearance—**CAD from Siemens** with intl clinical trial data & FDA clearance;[3]
- GE & Siemens has not cleared AI features with system[3]
- Philips NMPA submissions got rejected by NMPA mainly due to 1) Lacking of China-GCP compliant clinical trial evidence for CAD; 2)No Chinese population training dataset

BU	AI feature	Remark for NMPA rejection
MR	MRCAT-Brain	× No Chinese population in training dataset; china clinical study required.
EDI-ISP-12	ClearRead	× Requested to submit as SaMD
	LNA CAD	× No GCP compliant clinical study data
	CT Pulmo	× No GCP compliant clinical study data

Note: [1] "AI Medical Devices Registration Review Guidelines" (No.8, 2022), March 9, 2022"; [2] see appendix for details; [3]informal reg intelligence for GE/Siemens, not available on NMPA website

Definitions in Standards

ISO/IEC JTC1 SC42 is developing a series of standards for AI, across all industries. It is hoped that these standards can be used as the basis for sector-specific standards such as healthcare. Our details might be different, but the general concepts are (hopefully) the same (an earlier draft of this definition was considered by IMDRF.)

> AI System: Engineering system that generates outputs such as content, forecasts, recommendations or decisions for a given set of human-defined objectives.

What is AI ? Physicians Viewpoint…

"Artificial intelligence constitutes a host of computational methods that produce systems that perform tasks normally requiring human intelligence. These computational methods include, but are not limited to, machine **image recognition**, natural language processing, and machine learning. However, in health care a more appropriate term is "**augmented intelligence**" (AI), reflecting the enhanced capabilities of human clinical decision making when coupled with these computational methods and systems."

Augmented intelligence in health care (AMA Board of Trustees, 2018)

Terminology challenges: If you can't agree on what to call it, there's no way you can agree on what it should do

Artificial Intelligence practitioners have their own set of terminology that sometimes conflicts with what we think of in Health informatics.

- "AI" might mean multiple techniques that lead to 'intelligent' behavior, but is often used to talk specifically about "Machine Learning"
- "Validation" for medical devices often refers to meeting user needs; but "validation" in data science is making sure the data and model are valid.
- "Bias" is something that data scientists try to eliminate, but many caregivers want algorithms to be biased towards **their particular patient demographics**.
- "Supervised" learning sounds as if there is someone that is supervising the software as it is learning (like you supervise a new employee.) But data scientists use this to mean data that is labelled (vs. an unlabeled pile of information)

Why should I care?

Machines will not replace physicians but **physicians using AI will soon replace those not using it."**
AI-augmented multidisciplinary teams: hype or hope? (Di Ieva, 2019) The Lancet

"Interest in artificial intelligence in healthcare soared in 2019 with investors pouring $4 billion into the sector across 367 deals… That's up from nearly $2.7 billion invested in healthcare AI in 2018 across 264 deals." "Healthcare led AI investment, topping the $2.2 billion raised by financial and insurance AI."

Fierce Healthcare coverage of CB Insights Report

AI will be critical in meeting the care needs of a growing, aging population facing projected physician shortages. However, concerted effort is needed to assure this tech advances the quintuple aim.
National Academy of Medicine Report on AI (Matheny et al., 2019)

FIGURE S-1 | Advancing to the Quintuple Aim
SOURCE: Developed by publication editors

Example of FDA Cleared AI: IDx-DR
Screening retinal images to detect retinopathy

- Diabetic retinopathy is when high blood sugar levels damage blood vessels in retina
- Retinal images are uploaded to a cloud server where IDx-DR software analyzes and tells doctor “more than mild diabetic retinopathy detected; refer to an eye care professional” or “negative for more than mild diabetic retinopathy; rescreen in 12 months”
- Note that this product provides a screening decision without having the clinician also interpret the results, and is therefore usable by healthcare providers not normally involved in eye care.

Source: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604357.htm

Why now? What is driving this?

There have been several AI Winters in the past – why is AI warming up again? Why do we think this might be the last Winter?

Two + one reasons:

1. IoT / Big Data
2. Video games!
3. The IoMedical Things

Please consider the following:

Types of AI Applications in Healthcare

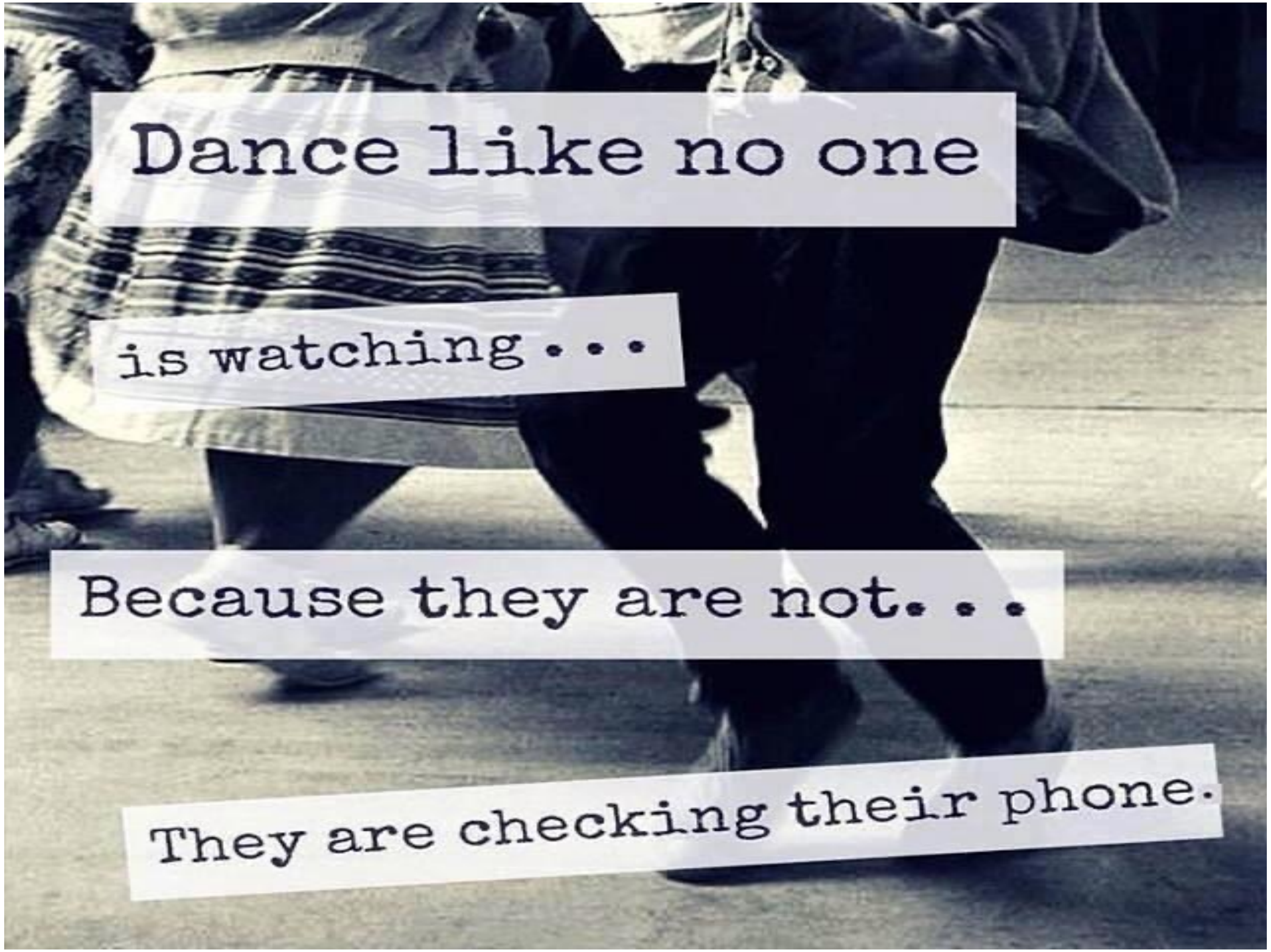
Artificial Intelligence will bring significant improvements to healthcare in many ways

- Improve diagnosis and effectiveness of therapy
- Managing population health
- Managing hospital operations
- Managing manufacturing operations
- Managing post-market activities

New Technology = New Risks

Pedestrian fatalities rose 11% in 2016, ‘distraction’ as a contributing factor.

As we gain new skills, what do we give up?



Model Diversification – Refinement & Drift

- Many of us have a long history of working in an environment that is slow to change, and therefore we offer a generic solution to meet common healthcare problems.
- However, with Continuously Learning Systems (CLS), the system **wants** to change. It wants to be customized for a particular customer. A CLS system can learn about a local population and can optimize for that particular hospital.
- But the manufacturer is responsible for configuration management and change control. The manufacturer is responsible for root cause analysis when something goes wrong and the application doesn't perform as it should.

Model Diversification – Refinement & Drift continued..

- **If every hospital is different, how can you compare performance? How do you handle performance claims that change over time**?

- DRIFT: Even if you lock a system and don't allow changes, patient populations **DO** change over time, and the performance you had 5 years ago might not be the level you are at today. Medical practice also changes over time and that may have an impact to performance.
  - **Therefore, having a completely locked system isn't necessarily the best idea either**…

Success Factor: Good Data Handling Practices

One challenge is that AI seems mysterious and magical, and people think we need a whole new way of thinking about it.

I propose that we handle data according to these rules:

- Keep records / retain information on the origin of the sample
- Sourcing, processing, preservation, testing and handling should be done in a safe manner
- Protect against contamination, viruses

Note: these concepts are already captured in IMDRF GRRP WGN47 FINAL:2018 document – when talking about tissue samples !!

Image source: https://xkcd.com/1838/

Levels of Autonomy

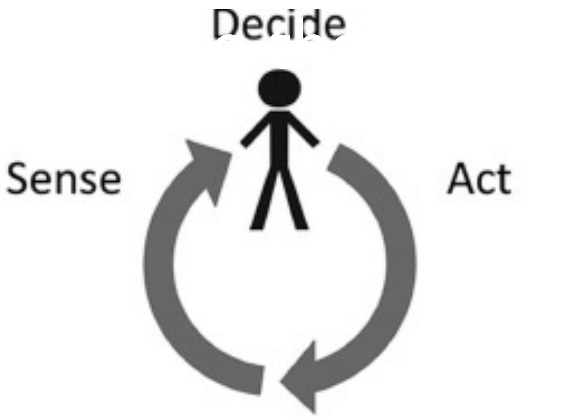
The automotive industry is also looking at autonomy -- this table is from an automotive standard,

SAE J3016

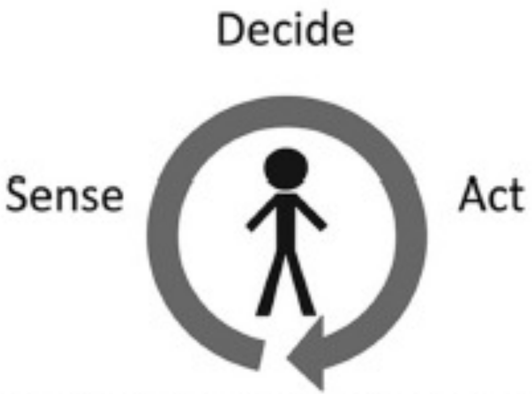
SAE level	Name	Narrative Definition	Execution of Steering and Acceleration/ Deceleration	*Monitoring* of Driving Environment	Fallback Performance of *Dynamic Driving Task*	System Capability *(Driving Modes)*
***Human driver* monitors the driving environment**						
0	**No Automation**	the full-time performance by the *human driver* of all aspects of the *dynamic driving task*, even when enhanced by warning or intervention systems	Human driver	Human driver	Human driver	n/a
1	**Driver Assistance**	the *driving mode*-specific execution by a driver assistance system of either steering or acceleration/deceleration using information about the driving environment and with the expectation that the *human driver* perform all remaining aspects of the *dynamic driving task*	Human driver and system	Human driver	Human driver	Some driving modes
2	**Partial Automation**	the *driving mode*-specific execution by one or more driver assistance systems of both steering and acceleration/ deceleration using information about the driving environment and with the expectation that the *human driver* perform all remaining aspects of the *dynamic driving task*	**System**	Human driver	Human driver	Some driving modes
***Automated driving system* ("system") monitors the driving environment**						
3	**Conditional Automation**	the *driving mode*-specific performance by an *automated driving system* of all aspects of the dynamic driving task with the expectation that the *human driver* will respond appropriately to a *request to intervene*	System	**System**	Human driver	Some driving modes
4	**High Automation**	the *driving mode*-specific performance by an automated driving system of all aspects of the *dynamic driving task*, even if a *human driver* does not respond appropriately to a *request to intervene*	System	System	**System**	Some driving modes
5	**Full Automation**	the full-time performance by an *automated driving system* of all aspects of the *dynamic driving task* under all roadway and environmental conditions that can be managed by a *human driver*	System	System	System	**All driving modes**

Loopy Humans - to what degree are "humans in the loop" ??

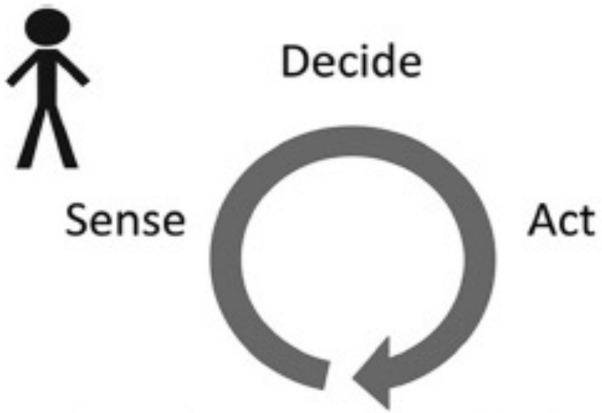
A simple model of Autonomy



The machine performs a task and then waits for the human user to take an action before continuing.



The machine can sense, decide, and act on its own. The human user supervises its operation and can intervene, if desired.



The machine can sense, decide, and act on its own. The human cannot intervene in a timely fashion.

FDA Position – AI/ML Enabled SaMD

Adaptive artificial intelligence and machine learning technologies differ from other software as a medical device (SaMD) in that they have the potential to adapt and optimize device performance in real-time to continuously improve health care for patients.

- The FDA is considering a total product lifecycle-based regulatory framework for these technologies that would allow for modifications to be made from real-world learning and adaptation, while still ensuring that the safety and effectiveness of the software as a medical device is maintained.

Good Machine Learning Practice Principles

The FDA, Health Canada, and MHRA published a draft set of GMLP Guiding Principles. These principles will help guide the development of future standards and regulations.

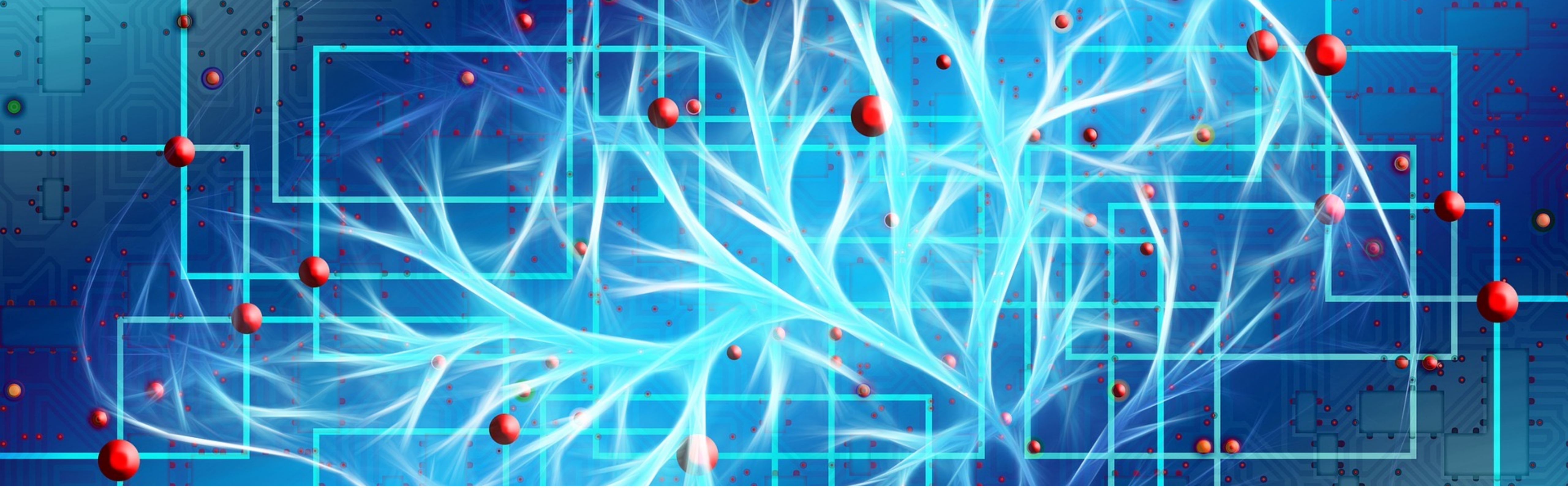
Good Machine Learning Practice for Medical Device Development: Guiding Principles	
Multi-Disciplinary Expertise are Leveraged Throughout the Total Product Life Cycle	Good Software Engineering and Security Practices are Implemented
Clinical Study Participants and Data Sets are Representative of the Intended Population	Training Data Sets are Independent of Test Sets
Selected Reference Datasets are Based Upon Best Available Methods	Model Design is Tailored to the Available Data and Reflects the Intended Use of the Device
Focus is Placed on the Performance of the Human-AI Team	Testing Demonstrates Device Performance during Clinically Relevant Conditions
Users are Provided Clear, Essential Information	Deployed Models are Monitored for Performance and Re-training Risks are Managed

TC215 Task Force 5 Application of AI to Health Informatics

In 2019, ISO/TC 215 started a project to assess the impact that AI will have on future TC215 projects, and after publishing the report, established a Task Force to help TC215 develop those standards.

TF5 has been created to (among other things..)

Develop Definitions
Maintain a Standards Landscape of what other committees are developing
Support use cases
Consider educational projects
Liaison and collaborate with other organizations.



Summary

We intend to continue Collaboration & Planning between ISO and IEC for Health informatics and AI Standards reflecting the “vertical domain of Health

We should be a chapter in the book of AI across all industries, not write our own book

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Thank you

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