Toward ontologies for imaging biomarkers description

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Goals of the presentation

- To introduce the key role of imaging biomarkers in the future
- To highlight the importance of sharing them for biomedical research
- To discuss the challenges of modelling them using ontologies

Overview

- Introduction (definition of imaging biomarkers)
- Part 1. Change of paradigm (led by imaging biomarkers)
- Part 2. Toward ontologies for imaging biomarkers
- Conclusion

Introduction

Definition

Imaging biomarkers

- Definition of biomarkers (Atkinson 2001)*
  - « characteristics that are objectively measured and evaluated as indicators of
    - normal biological processes,
    - pathological processes,
    - pharmaceutical responses to a therapeutic intervention »
- Definition of (quantitative) imaging biomarkers
  - Derived from medical images
  - Quantitative, objective, reproducible
  - « qualified » for specific clinical uses

** Clin Pharmacol & Ther. 2001 Mar;69(3):89-95. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Biomarkers Definitions Working Group.*

Imaging biomarkers

- Used for
  - Early detection of disease
  - Staging and grading
  - Predicting response to treatment
  - Assessing response to treatment

Imaging biomarkers

Insights Imaging (2013) 4:147–152
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STATEMENT

ESR statement on the stepwise development of imaging biomarkers

European Society of Radiology (ESR)

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Paper prepared by the ESR Subcommittee on Imaging Biomarkers (chairperson: Bernard Van Beers)

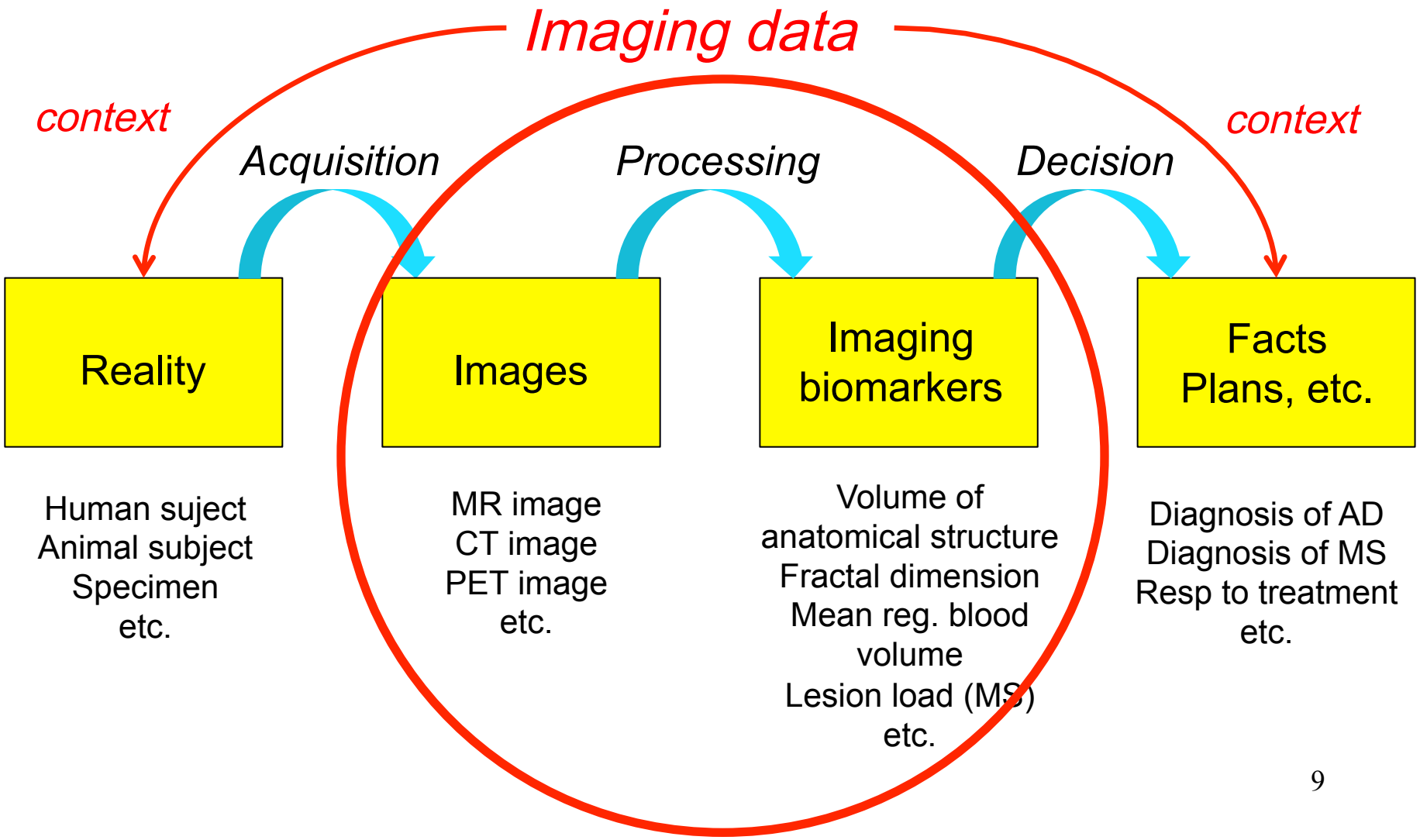
Imaging biomarkers

- Of critical importance in research, now
  - Focused clinical research (e.g. controlled clinical trials)
    - Used as « surrogate endpoints » (in place of clinical endpoints)
  - Translational research
    - Link/correlate results obtained in various domains

  → Key aspect of future federated imaging biobanks
- Of critical importance in individual patient management (decision criteria), in the future
  - Diagnosis, prognosis, treatment

  → Key aspect of a structured EHR / tasks planning

General framework



Imaging biobanks

- A new concept to enable a wide-scale sharing of images and imaging biomarkers for biomedical research
  - ESR established a new WG on « imaging biobanks »
    - To promote standardisation, validation and benchmarking of imaging data (incl. imaging biomarkers)
    - To stimulate linking and integration of existing (national and regional) image repositories
    - To stimulate linking imaging biobanks and traditional biobanks

Motivations for an ontology of imaging information

- Data sharing in federated imaging biobanks
  - Convergence of information models
  - Mediation between heterogeneous models
- Reasoning / decision models based on biomarkers (biological and imaging biomarkers)
  - Diagnosis
  - Staging and grading
  - Prognosis
  - Treatment

Part 2. Towards ontologies for imaging biomarkers

Domain to be covered

- Images acquired on humans, animals or specimen
- Data obtained by processing of the latter
  - Images, e.g. denoised images, template resampled images, statistical maps etc.
  - Parts of images (ROI), e.g. binary or probabilistic masks (segmentation results), graphs (e.g. contours, tractography data, 3D surfaces, meshes)
  - Measurements derived from image data (imaging biomarkers)
- Metadata associated to the latter data …

Metadata associated to imaging data

- Data identifiers
- Data class taxonomy
- Data format (when relevant)
- Relation to a container or access resource
- Data provenance
  - Result of some acquisition , i.e. process involving some physical interaction with the subject or sample (equipment, protocol and acquisition parameters)
  - Result of some data processing (processing tool, input data, output data, parameters)

Metadata associated to imaging data

- Relation to the subject and / or sample
  - State of the subject during data acquisition (e.g. injected tracer, activation paradigm)
  - Role played by, e.g., an imaging biomarker
- Relation to the study which motivated data creation
- Relation to other data related the same subject, that may need to be correlated with images
  - Clinical data (surgery, radiotherapy, etc)
  - Neuropsy or behavioural scores
  - Genomic and other omics data

Principal ontologies (and information models) to start from

- Foundational ontologies: BFO or DOLCE
  - Provide a common modeling framework as well as the major top-level entities
- Measurement and information artifacts: OBI / IAO
- Qualities: PATO
- Provenance: PROV
- Imaging: RadLex, AIM, OME
- Imaging datasets: OntoNeuroLog
- Imaging biomarkers: QIBO
- Medicine in general: SNOMED, ICD, NCIT

But of inequal quality and completeness

Existing ontologies: OBI / IAO

Ontology of Biomedical Investigation / Information Artefacts Ontology

- Good
  - Based on BFO
  - Basic entities for representing *Information content entity*
  - Interesting taxonomies for *measurement data items* and *data transformations*
  - relation to measurement processes (*assay*) and measured quality
  - Well-documented
- Bad
  - No detailed taxonomy of images (limited to projection images ?)
  - No taxonomy of image formats
  - No detailed taxonomy of *imaging assay* nor *image creation device*

Existing ontologies: RadLex

Radiology Lexicon

- Good
  - Very broad lexicon
  - Taxonomy of *procedure steps, contrast agents, radiopharmaceuticals*
  - Taxonomy of *(Radlex) descriptors*

- Bad
  - Not based on an upper level ontology
  - No clean separation between information content entity and real world entities
  - No taxonomy of image formats
  - OWL representation very complex (metaclasses)

Existing ontologies: ONL-DP

OntoNeuroLOG – Dataset Processing (also imports dataset)

- Good
  - Based on DOLCE
  - Taxonomy of *Dataset* (quite complete for MR only)
  - Taxonomy of *Dataset processing*
  - Taxonomy of *Image formats*
  - Solid model of contextual entities: *Study*, *Subject*, *Examination*…
- Bad
  - Needs a more formal definition of image datasets (w.r.t. measurement and mapping to space)
  - Multiple inheritance needs revisiting (equivalent class axioms)

Existing ontologies: OME

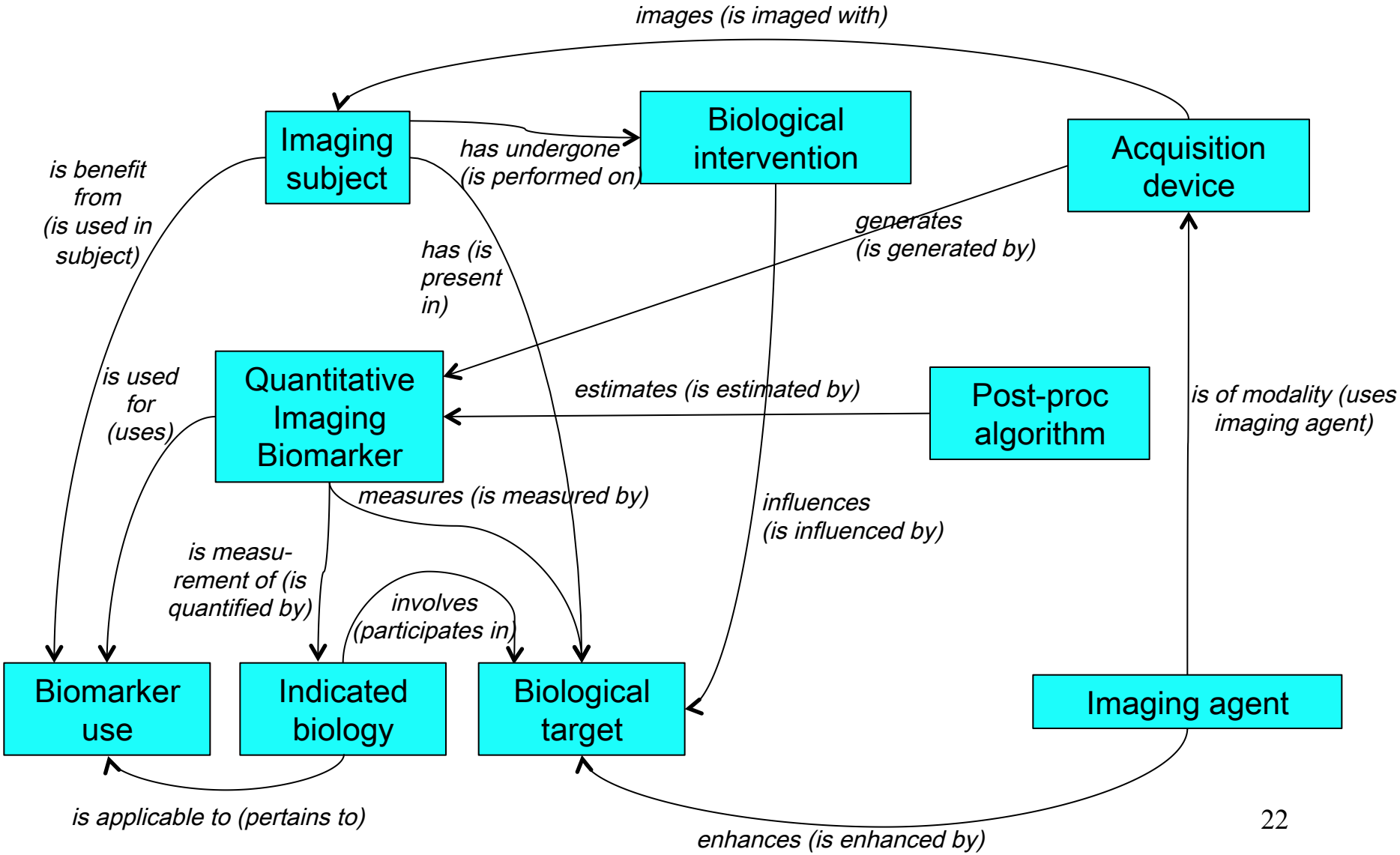
Open Microscopy Environment

- Good
  - Model of image (5D structure based on basic 2D frames)
    - 2D frames (x,y) + focus (z) + wavelength or channel (c), and time (t)
  - Complete schema of contextual entities : *Project*, *Experiment*, *Instrument*, etc.
  - Use of the Life Science ID (LSID)
- Bad
  - XML data model rather than ontology
  - Not based on an upper level ontology

Existing ontologies: QIBO
(Quantitative Imaging Biomarkers Ontology)

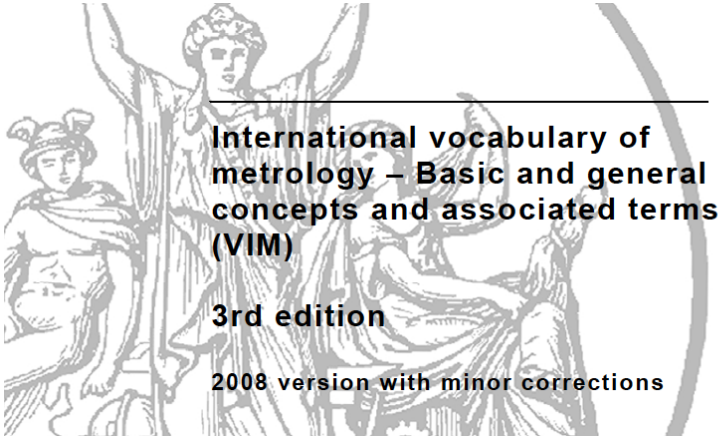
- Good
  - Taxonomy of *imaging subject*
  - Taxonomy of *biological targets* (of *imaging agents*)
    - (Molecular Imaging and Contrast Agent Database – MICAD)
- Bad
  - Not based on an upper level ontology, nor relevant ontologies
  - No taxonomy of usal biomarkers
  - Poor documentation (OWL implementation not consistent with JDI paper of 2013)
  - Objects properties are defined but never used

Main entities introduced in QIBO



Gaps and open issues (1/4)

- Need for a consistent modeling of measurements, suitable for
  - Images
  - Imaging biomarkers
- Addressing
  - Measured quality
  - Relation to object / process being measured
  - Provenance (measurement process, participating entities, acquisition versus data processing, etc)



Gaps and open issues (2/4)

- Need for adequate representational entities for entities such as regions of interest (ROIs)
  - means to relate them to real world entities
    - Semantically-neutral reference: (is about / *refers to*)
    - or more precise semantics: *delimits exactly*, *overlaps*
  - Should be valid across all domains of imaging (radiology, molecular imaging, microscopy, etc)

Gaps and open issues (3/4)

- Basic ontological nature of imaging biomarker: actual measurement derived from images ? or instrument designed to produce reliable and reproducible measurements

- Both aspects are relevant
  - The first with respect to the actual use of biomarkers in image management (e.g. image retrieval and reuse)
  - The second with respect to the qualification processes, reuse of image processing for user purposes

Gaps and open issues (4/4)

- Need to distinguish between
  - imaging biomarkers as results of some measurement
  - And their role or function in patient management

Agenda (1/2)

- Develop/extend the relevant domain ontologies based on needs of specific application domains
  - Needs to involve relevant domain experts
    - radiological specialities (e.g. cancer, neuro, cardio)
    - DICOM standard community
    - the editors of major image processing packages
  - as well as ontologists
- Assess and consolidate core ontologies such as OBI/IAO, PATO, etc.

Agenda (2/2)

- Deploy experimental systems in research infrastructures and imaging biobanks first.
  - Get feedback from researchers
- Then, consider deployment into clinical PACS, to support
  - Intelligent task management systems (workflow)
  - Decision support systems
  - Quality management systems

Conclusion / Summary

- We underlined the importance of imaging biomarkers in research (both clinical and translational research) and care delivery
- We underlined the importance of developing and federating imaging biobanks to share and reuse them in biomedical research
- And finally we reviewed and discussed existing ontologies that might be used toward an ontology of imaging biomarkers

Thank you for your attention