NEI-FDA-ONC Joint Workshop on Promoting Adoption of Ocular Imaging Standards

Virtual Workshop

May 10, 2022

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Table of Contents

Meeting Summary

Session 1: Where Are We Now and Where Do We Want to Be?

Moderator: Kerry Goetz, MS, National Eye Institute

Introduction and National Eye Institute Perspective

Michael F. Chiang, M.D., Director, National Eye Institute

Founded in 1968 and charged with managing national efforts in vision science, the National Eye Institute (NEI) has an annual budget of $863M and is a world leader in directing and funding eye and vision research. NEI's mission is to eliminate vision loss and improve quality of life through vision research, and its 2021-2025 strategic plan emphasizes innovation through data science, data sharing, collaboration, and population health. As a field, ophthalmology has taken a leading role in artificial intelligence (AI) and data science integration. Access to a wide spectrum of biology, imaging, clinical, and public health data primes vision research for immense potential to leverage data science. However, these opportunities require interoperability to support broad data sharing and access to raw data from devices. Currently, a lack of standards adoption challenges the field, impeding exchange of ocular imaging data, reducing image management efficiency in clinical settings, and preventing researchers from accessing image data or quantitative metrics. Gaps in interoperability hinder the field's ability to innovate, serve patients, and conduct vision-saving research.

Efforts toward standardization in ophthalmology have followed the example set by the field of radiology's Digital Imaging and Communications in Medicine (DICOM®) standard. The American Academy of Ophthalmology (AAO) formed DICOM Working Group 9 (WG-09) on ophthalmology standards in 1998, which developed standards for all common image modalities. Despite more than two decades of diverse AAO efforts to establish a universal ocular imaging standard, publications and policy statements during this time have generated little progress toward fuller adoption of DICOM Version 3.0. To assess this need, NEI issued a Request for Information regarding ocular imaging standards in February 2022 and published an executive summary of the comments received on May 6, 2022.

NEI, the U.S. Food and Drug Administration (FDA), and the Office of the National Coordinator for Health Information Technology (ONC) jointly supported this workshop to develop and implement a plan to improve vision research and clinical care through ocular imaging standards adoption. The goal of this workshop was to convene a wide variety of participants including researchers; clinicians; policymakers; and representatives of vendors, government, other research sponsors, and professional societies to collaboratively identify barriers and approaches toward widespread adoption of standards for interoperability in ophthalmology.

Radiology's Experience

Charles E. Kahn, Jr., MD, MS, University of Pennsylvania

The American College of Radiology (ACR) and National Electrical Manufacturers Association (NEMA) formed a joint committee in 1983 to address interoperability among systems that generate, display, and store medical images. Ten years later, in 1993, this partnership of users and manufacturers became DICOM: Digital Imaging and Communications in Medicine. DICOM offers a mechanism for the interchange of information that underpins virtually every device in radiology: there are hundreds of thousands of medical imaging devices and tens of billions of DICOM images worldwide. DICOM provides for the transmission and persistence of complete objects (e.g., images, waveforms, documents), allows for the query and retrieval of those objects, defines specific actions, provides workflow management, and ensures quality and consistency of image appearance. DICOM's governance reflects the partnership that anchors the standard: the DICOM Standards Committee includes medical organizations, equipment manufacturers, and others; elected leadership comprises a user co-chair and an industry co-chair; and NEMA staff serve as secretariat.

In radiology, DICOM has improved clinical practice and has accelerated AI readiness by enabling the retrieval, manipulation, and information capture of digital images. DICOM enhances CT and magnetic resonance objects with multiframe functional groups that eliminate repeated header information to increase bandwidth and storage efficiency. DICOM augments image visualization capacities through the combination of 2D images into multiframe objects, segmentation of 2D composite data, polygonal shape descriptions of 3D data, and 3D rendering and visualization. Further, DICOM improves radiological image quality by ensuring consistent appearance of images on film and display monitors and consistent presentation of information through tools, such as magnification, window-level adjustments, and image processing. DICOM belongs to the International Organization for Standardization (ISO) and works closely with other standards bodies, including the American National Standards Institute, Health Level Seven International, and Integrating the Healthcare Enterprise.

Radiology also has adopted semantic standards to drive progress toward standardization. These standards include a shared radiology lexicon (RadLex®), common data elements, and radiology report templates to standardize terminology usage, ensure consistent presentation, and increase data availability for secondary uses in quality assurance and research.

Imaging Standards: The Value of Interoperability

Krishna Juluru, MD, National Institute of Biomedical Imaging and Bioengineering

Standards such as DICOM (ISO 12052:2017) improve efficiency and accessibility in varied industries. The DICOM standard facilitates interoperability of medical imaging equipment by specifying protocols for network communications; syntax and semantics of information exchanged using those protocols; a set of media storage services, file format, and medical directory structure for media communication; and information to be supplied. In contrast, DICOM does not specify the implementation details of any features of the DICOM standard; the

overall set of features and functions to be expected from a system of integrated DICOM-compliant devices; or a testing/validation procedure to assess DICOM conformance.
DICOM can be used to store a variety of information, including primary and secondary capture images, textual and numeric data, and annotations. Individual DICOM files contain a header that includes rich metadata (e.g., study date and time, series date and time, manufacturer, modality) to facilitate Picture Archiving and Communication System (PACS) sorting. Ocular imaging can benefit from the use of both DICOM segmentation objects, which store object contour information in the native coordinate environment for machine analysis, and DICOM structured reports, which contain textual and numeric data. DICOM structured reports store annotations, segmentations, and data derived from image processing discretely and accessibly, and offer a superior alternative to archiving that information in secondary capture images for extraction using optical character recognition, which often results in errors.

Improving interoperability among DICOM-compliant systems requires increased agreement on the aspects of implementation, integration, and testing and validation that the DICOM standard does not specify. Key actions to promote that agreement include building relationships among professional societies, standards bodies, vendors, and regulators; focusing on the efficiency and research quality gains that improved workflows and connectivity systems can enable; and developing a Connectathon culture that regularly brings stakeholders together to test conformance and respond to the evolving needs of ocular imaging. Effective collaboration with vendors also requires ensuring that conformance to standards and interoperability increases the value of proprietary technologies.

My 15-Year Saga of Integrating Clinical Imaging Using Standards

Michael V. Boland, MD, PhD, Harvard Medical School; Massachusetts Eye and Ear

Vendor implementation of the DICOM standards for ophthalmology developed by WG-09 offers important benefits for clinical practice; however, little progress has been made toward broad adoption of these standards in recent years. Implementation of DICOM supplements varies among individual vendors and functional interoperability across vendor platforms remains limited. Increasing standards adoption and interoperability is essential to patient safety and efficiency. Patient demographics should be shared across all systems and easy to access at the point of care to reduce records variance and errors, avoid testing redundancy, and support clinical decisions.

Dr. Boland deployed a DICOM workflow to integrate imagining in a clinical setting to view multiple test results simultaneously and interact with the data generated. Within the workflow, electronic health records (EHRs) feed patient demographics into a DICOM work list that is sent to testing devices to link demographics to DICOM image and data outputs, which are then sent to PACS (a medical image storage and archive hub) for review on connected devices. To assess the outcome of implementation, Dr. Boland piloted the DICOM workflow in the glaucoma service within a large ophthalmological practice. Prior to implementation, 9.2 percent of images were misfiled and required intervention. The proportion of misfiled images had decreased to 4.3 percent at 3 months following workflow implementation and to 1.4 percent at 6 months

following implementation, representing a significant benefit in resources and time saved. Dr. Boland then deployed the DICOM workflow across a large practice with dozens of devices and many locations. This expansion required coordination with vendors to ensure all devices could integrate with the DICOM work list and send DICOM data outputs to PACS. Although the data integration required presented challenges, every major ophthalmology vendor was able to provide the necessary level of functionality for integration into the workflow.

Advancing interoperability in ocular imaging requires specifically delineating the needs and standards that vendors should meet to ensure efficient progress. Clinical needs include increased adoption of key DICOM supplements (e.g., tomography, macular thickness, axial length/biometry); the development of viewers that work across platforms, which may require FDA approval; and enhanced ability to move DICOM objects between systems in support of shared or transferred care. Vision science research would benefit from improved ease of extracting DICOM objects in bulk for analysis.

Why Do Ocular Imaging Standards Matter for Vision Science Research?

Aaron Y. Lee, MD, MSCI, University of Washington

Research in ophthalmological applications of AI deep learning has rapidly developed in recent years. Accelerating deep learning in vision science research requires the curation of large-scale imaging datasets and increased adoption of ocular imaging standards. In 2015, Dr. Lee found that translating binary data elements contained in optical coherence tomography (OCT) imaging SDB files into grayscale values generated an image that approximated an OCT B-scan. Dr. Lee developed a Python script to extract all OCT imaging ever done at the University of Washington, en masse. Using Epic Clarity data, Dr. Lee linked deidentified images with clinical information to create a database of approximately 5 million OCT B-scans representing a decade of clinical practice. This led to the development of an automated binary classification model to identify pathology in OCT B-scans. Notably, the vast majority of the time and effort needed to achieve automated extraction was devoted to data sourcing and cleaning. In total, Dr. Lee spent 1 year creating the database—training the deep learning model required only 2 days of that time.

Dr. Lee's experience illustrates the potential of scalable deep learning algorithms to quickly leverage large quantities of data once access and formatting challenges have been resolved. Ocular imaging standards adoption can advance AI-driven innovation in vision science research by facilitating access to the tens of thousands if not millions of standardized images needed to train machine learning (ML) models. The Heidelberg Engineering HEYEX 2 system represents a meaningful step toward DICOM adoption as it enables viewing of ophthalmic images in DCM format (the common file format used to store medical imaging data when a patient undergoes many types of medical scans) across many devices with accurate metadata and image display. Productive steps toward broader standards adoption and improved data accessibility for AI applications could include (1) vendor use of DCM files that can be opened in third-party viewers and include images in the pixel array rather than merely encoded in the DICOM header; (2) storage of key metrics from segmentation algorithms as discrete structured data elements in the

DICOM header or structured report for EHR and researcher access; and (3) renewed and consistent efforts to extend, maintain, and implement future DICOM standards.

Imaging Data Standards in Clinical Research for Ophthalmology: Challenges to Enable Impact-Driven Data Mastery

Daniela Ferrara, MD, PhD, MS, Genentech; Tufts University

Clinical research in ophthalmology relies on image analysis that provides insights into physiopathological mechanisms, disease and patient population categorization, therapeutic target discovery, and assessment of safety and efficacy of new therapies. Maximizing the usefulness of ocular imaging data requires linking to population-level and longitudinal data from varied, decentralized sources (e.g., visual function tests, clinical records, wearables, genetics). Gaps in data standardization and metadata present integration challenges for both clinical trials and practice. Even when ocular imaging data is available in nonproprietary formats, lack of adequate metadata interferes with organization, automation, and scalability.

These challenges impact data acquisition, management, and analysis, with consequences including increased costs, delayed scientific discoveries, and heightened risk of errors that could impact patient safety and privacy. Further, lack of access to standardized, structured, interoperable data compromises the ophthalmological field's ability to manage big data efficiently and leverage AI tools to accelerate scientific discoveries. Although the adoption of ocular imaging standards will not independently resolve all challenges, increased collaboration and implementation of standards among imaging device manufacturers can enhance the ophthalmological community's ability to take advantage of technological advancements, engage new stakeholders in the ocular imaging ecosystem, and improve patient care.

Session 2: What Do We Need to Reach the "Vision for the Future"?

Moderator: Amberlynn Reed, MPH, NEI

U.S. Food and Drug Administration Device Interoperability

Elvin Ng, FDA

FDA regulates a variety of ophthalmological devices, including software as a medical device (SaMD), defined as software that is integral to a medical device, and software in a medical device (SiMD), defined as software intended to be used for one or more medical purposes that performs these purposes without being part of a hardware medical device. Per the 21st Century Cures Act, FDA oversight no longer includes medical device data systems (MDDS), medical image storage devices, or medical image communication devices. The medical devices FDA has oversight over typically rely on large volumes of information to achieve their intended use. Thus, the FDA Center for Devices and Radiological Health attends carefully to the inputs a medical device requires and the outputs it generates. In ophthalmological devices, these outputs include images, scans, measurements, and segmentations. As use of AI in diagnostic software increases, hardware imaging device outputs are now also commonly used as inputs for analysis.

Safe and effective SaMD requires demonstrated performance of the software with the devices it is indicated for, underscoring the importance of interoperability between medical devices. The increasing connection of electronic medical devices to each other and other technologies heightens the need for connected systems to safely, effectively, and securely exchange and use information. FDA believes that increased medical device interoperability can improve patient care, reduce errors and adverse events, encourage innovation, and facilitate more diverse study datasets. Open availability of the functional, performance, and interface requirements of interoperable devices (e.g., through labeling) can minimize potential problems or misuse.

FDA has recognized several standards related to interoperability, published an interoperability guidance document in 2017 and supports efforts to increase interoperability such as the Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD) initiative to promote a uniform laboratory reporting structure. On April 22, 2022, FDA formally recognized the DICOM standard and WG-09 supplements for ophthalmic devices. Although conformance with recognized consensus standards is voluntary for medical device manufacturers, FDA recognition of design standards that support interoperability encourages manufacturers, health care organizations, and others to implement interoperability in a standard fashion. In addition to device interoperability, standards adoption can also improve data standardization and thus increase the potential of real-world data sources such as the AAO's IRIS Registry to advance regulatory science for ophthalmological devices.

Office of the National Coordinator for Health Information Technology Interoperability with Electronic Health Records

Andrew Northup, ONC

Established in 2004 and legislatively mandated in 2009, ONC is charged with the coordination of nationwide efforts to implement and use the most advanced health IT and the electronic exchange of health information. To sever this objective, ONC conducts standards, certification, and exchange activities. Standards activities include the maintenance of health data classes and data elements to facilitate interoperability and shareable data through the United States Core Data for Interoperability (USCDI) and Interoperability Standards Advisory (ISA). ONC's voluntary certification program catalogs products that meet requirements established by standards, implementation specifications, and HHS criteria on the Certified Health IT Product List. In its coordination of the electronic exchange of health information, ONC promotes the adoption and implementation of standards by accelerating application program interfaces (APIs), supporting the creation of Health Information Exchanges, and developing the Trusted Exchange Framework and Common Agreement.

The ISA lists the applicable standards and implementation specifications that exist for use cases and domains throughout health care, providing a resource to help identify standards, code systems, and value sets that can further the goals of specific health care domains or specialty areas. In the ISA, DICOM is classified as a content standard for use cases related to exchange of image data. DICOM is the only standard listed for the Format of Medical Imaging Reports for

Exchange and Distribution Use Case. DICOM also appears in other use cases within the ISA, such as the Format of Radiation Exposure Dose Reports for Exchange and Distribution, because DICOM structured reports contain metadata about the machine a scan was performed on, its characteristics, and its use of ion radiation-generating modalities.
The web-based version of the ISA is updated frequently with input from stakeholders in industry and beyond to reflect the current standards available for use cases. Registered users can propose modifications by submitting a new ISA element for consideration. ONC also publishes a PDF Reference Edition of the ISA each December, and annually solicits review and comments in support of that version.

U.S. Core Data for Interoperability

Albert Taylor, MD, ONC

ONC developed the USCDI, a set of structured and unstructured core data elements that support patient care and patient access to data, to advance the implementation of health IT standards. The USDCI provides a consistent, reliable baseline of harmonized data elements that can be referenced across use cases, including those outside of patient care and patient access. The health data contained in the USCDI is expressed in Certified Health IT modules and exchanged using specific standards, such as Fast Healthcare Interoperability Resources (FHIR). USCDI data elements represent individual concepts (e.g., medications, allergies, health concerns), and some require expression using specific health IT vocabulary standards (e.g., RxNorm or Systemized Nomenclature of Medicine – Clinical Terms). The USCDI does not specify criteria for health data exchange or exact content format. Per the 2020 ONC Cures Act Final Rule, ONC's voluntary EHR certification program requires USCDI version 1 capture using FHIR US Core and consolidated clinical document architecture exchange. The USCDI currently defines the set of data expected to be collected and exchanged between EHR systems and to which information blocking penalties apply.

In addition to patient care and access, USCDI data can be used for various health care use cases, including interoperability, shared care planning, device data, research, and public and population health. The USCDI expands annually through public stakeholder input in a predictable, transparent, and collaborative process that weighs both anticipated benefits and industry-wide impacts. The submission period typically ends in September and ONC publishes the new version of the USCDI in July of the following year. USCDI version 1 replaced the Common Clinical Data Set and included the addition of clinical notes and provenance. USCDI version 2 added several new categories of information as well as new data elements related to sexual orientation, gender identity, and social determinants of health. In January 2022, ONC published a draft of USCDI version 3, which adds two new data classes (health status and health insurance information) and additional data elements related to patient demographics (e.g., tribal affiliation, occupation). ONC is currently evaluating comments received on the draft and will publish the final USCDI version 3 in July. ONC also offers a voluntary Standards Version Advancement Process (SVAP) that allows developers to update health IT to more recently published standards than those required for certified health IT. In June 2022, ONC will announce approved SVAP standards for 2022, potentially to include USCDI version 2 and other standards.

Discussion with Session 1 and 2 Presenters

Moderator: Amberlynn Reed, MPH, National Eye Institute

Potential for Deep Learning to Clone Proprietary Algorithms

Deep learning models can be used to clone algorithms using exported proprietary labels, potentially impacting vendor investment in algorithm development. Dr. Lee emphasized that although deep learning can use inputs and outputs to clone algorithms, advocating for fuller implementation of ocular imaging standards is not an endorsement of algorithm cloning. Dr. Lee added that rapid advances in AI technology have likely raised parallel issues in other fields of medicine, which may provide useful models to approaching concerns about algorithm cloning. Dr. Kahn noted that, in radiology, the DICOM standard facilitates display and interoperability of the results of manufacturer's proprietary segmentations but does not render the algorithm that produces that segmentation transparent. FDA oversight may help mitigate concerns about commercializing cloned algorithms in certain cases. Devices with functionality related to advanced image processing and segmentation are regulated under FDA oversight; MDDSs (Medical Device Data Systems) are not.

Access to Raw Data

Vendor manipulation of spectrometer data to generate images for display skews certain data (e.g., layer intensity) that may be of interest to researchers for algorithm development. Although including raw data on a routine clinical basis is not feasible due to storage demands, Dr. Lee suggested that researchers could partner with individual vendors to access raw data.

Needs Beyond the Scope of DICOM

Participants agreed that although DICOM implementation is not a comprehensive solution to all challenges in data management, ocular imaging standards adoption presents an opportunity to address many key barriers and promote collaboration. Federal data standards (e.g., USCDI) and Integrated Healthcare Enterprise (IHE) efforts to establish standards integration profiles can enhance the application of the international DICOM standard in the United States.

Session 3: Panel Discussion—How to Address Barriers to Adoption of DICOM

Moderator: Kerry Goetz, MS, National Eye Institute

Interoperability Needs for Clinical Practice and Research

Review Software and PACS Interoperability

Improved interoperability is needed among individual vendors' review software and between vendor review software and PACS. Dr. Elizabeth Murphy noted that although vendor software allows image transfer between systems, it does not facilitate analysis of images from another

vendor. Thus, clinics must maintain review software for all vendors for clinician use in every location. Availability of analysis tools across vendor review software would improve efficiency. CPT Boonkit Purt, MD, added that clinicians should be able to launch vendor-specific review software from any PACS, rather than needing to search for patients within individual vendors' software. Dr. Emily Chew noted that radiology uses a standardized PACS, whereas the lack of standardization in ophthalmology prevents contributions to image databases that can improve patient care and clinical research.

Dr. Raymond Iezzi noted that PACS development is hindered by vendors storing data in encrypted formats rather than complying with DICOM. Encryption forces PACS developers to reverse engineer proprietary data formats by reconstructing OCT displays and attempting to infer measurements. As a result, PACS integration of images from certain vendors do not display normally and lack measurements. CPT Purt agreed that OCT scan pixel data should be available in a publicly readable format and added that all structured data needed to regenerate a PDF scan report should be taggable and stored in DICOM format. Dr. Joel Schuman emphasized that information quality should be included as a tag parameter.

Comparison of Quantitative Results

Measurements are not standardized across devices; thus, differences in pixel size and signal processing can result in inconsistent measures. Dr. Schuman noted that vendor software does not currently allow clinicians to directly compare actual quantitative OCT results across devices from different manufacturers. Normalizing measurements based on signal amplitude and wavelengths would benefit patients and clinicians. Manufacturers could allow third-party processing of signal data to facilitate the normalization and comparison of OCT results, enabling testing for progression regardless of which device was used in previous patient scans.

Data Access, Deidentification, and Standardization

Panelists agreed that access to raw spectrometer data or minimally processed data is essential to both AI development and research use. Dr. Schuman noted that volumetric data provides more accurate predictions than segmentation data and enables feature-agnostic AI development. Dr. Kaushal Solanki added that the ability to communicate bidirectionally with vendor devices to allow AI tools to assess whether image quality and coverage are suitable for diagnosis would advance the development of autonomous AI systems. Dr. Murphy noted that the ability to export and deidentify raw data in batches at the patient level is important to facilitate both research and AI uses. Dr. Iezzi added that industry could provide software tools to convert large datasets for research purposes.

Dr. Emily Chew noted that NEI encountered significant costs and challenges in standardizing digitized photographs from a longitudinal study of 4,000 patients. Access to raw data that can be standardized at the time they are obtained would improve efficiency. LTC Marcus Colyer, MD, added that NEI's curated dataset represents a powerful resource that could serve as a baseline for interoperability of data across vendor platforms. Dr. Eddy Anglade suggested that discrete data collected in a randomized, prospective fashion for ophthalmological industry trials and

collaborative studies (e.g., DRCR Retina Network) could also be leveraged in support of data standardization efforts.

EHR Integration

Digital OCT and visual field data cannot be easily transferred from the acquisition device to a text based EHR, which hampers patient care. Dr. Schuman noted that accessible, exportable standardized OCT and visual function data of interest would facilitate assessment of the effects of medications and surgical interventions on individual patients, and potentially at a population level, through interoperability with the EHR.

Usability of Standardized Processes

CPT Purt noted that wide adoption of interoperable standards requires systems that are accessible to end users. If standardized processes increase burden, physicians and technicians are unlikely to implement them. For example, the DICOM standard workflow for ordering images is more burdensome compared to the IHE Unified Eye Care Workflow's encounter-based imaging.

Challenges and Opportunities in Standardization for Manufacturers

Need for Consensus

Panelists agreed that effective standardization requires market collaboration to identify needs and priorities in support of the shared goal to improve health. Vendors such as Heidelberg Engineering, Topcon Healthcare, and Zeiss are working toward increased interoperability and DICOM compliance. Dr. Niranchana Manivannan emphasized that consensus must be reached among academic researchers, clinicians, and industry, including not only ophthalmic device manufacturers, but also EHR and PACS vendors. Mr. Juho Uotila noted that the DICOM standard for ophthalmology emphasizes clinical practice and decision support and does not describe how raw data should be presented in depth. Priority software functions to serve clinical and research community needs differ in certain cases, which makes developing a vendor-neutral clinical platform to serve both communities more challenging.

Panelists also acknowledged the need to balance the attainment of consensus on standards with the delivery to market of technological innovations that can support the field's rapid progress. Dr. Manivannan noted that improved patient management should occur alongside standards development and implementation.

Deployment Challenges

OCT imaging, and particularly OCT angiography (OCT-A) contains large amounts of data. Mr. Reisman noted that bandwidth and storage have not kept pace with dataset requirements in some locations, and that vendors rely on investment in these capacities both in the United States and globally. Dr. Naama Hammel added that infrastructure gaps present application program

interface (API) deployment challenges. Variability in IT and electronic medical record systems across countries and clinics present barriers that standardization can help overcome.

Improving Accessibility of Historical Device Data

Exporting data from historical devices across manufacturers presents significant challenges because many historical devices have not received software updates in years. In some cases, migrating to newer software (e.g., from HEYEX 1 to HEYEX 2) can allow export of historical data. CPT Purt suggested that manufacturers could provide encoding specifications for devices they do not intend to update or maintain in order to allow the community to build open-source solutions to export historical data. Dr. Manivannan added that leveraging historical data requires considering the specific purposes patients consented to when providing the data.

Implementation Inertia

Mr. Uotila noted that a lack of standards uptake in the field disincentivizes manufacturers to take steps toward implementation while no demand for it exists. For example, because no viewers support OCT-A as a modality in the presentation it requires, device manufacturers have no incentive to create an output that conforms to the DICOM standard for OCT-A. Dr. Anglade suggested that the recency of OCT-A may facilitate pre-competitive collaboration among software and hardware manufacturers to develop a standard that leverages DICOM standardization and provides the outputs the community requires.

AI Integration for Biomarker Discovery

Vendors can advance biomarker discovery by providing researchers and AI applications access to image data. Dr. Reisman noted that later this year Heidelberg plans to bring a workflow to market that will allow AI applications to securely link to its datasets, and that the development of such solutions can also alleviate the regulatory and commercial burden that device manufacturers often bear to incorporate AI applications into devices. Dr. Solanki emphasized the importance of tags and digital signatures to ensure AI can be integrated into standards and workflows to create and validate biomarkers with real-world data. Dr. Hammel added that AI developers generalize to multiple devices in multiple settings, when possible, particularly for validation on test sets from different devices.

Approaches to Enhance Collaboration

Improving collaboration among clinicians, researchers, and vendors requires a culture that promotes sharing of large quantities of data. Drs. Iezzi and Solanki noted that effecting a shift in culture entails working with vendors to better understand the factors that motivate use of proprietary formats and ensuring that sharing tools and data can mutually benefit all stakeholders. CPT Purt suggested that a standards working group could facilitate the development of an accessible central repository for private DICOM tags. Dr. Manivannan added that vendors should not only support standards adoption, but also participate actively in cross-vendor events that engage the community, such as Connectathons.

Session 4: Panel Discussion—Evaluating Meaningful Adoption and What Else Is Needed (Beyond DICOM)

Moderator: Afrouz Anderson, PhD, National Institute of Biomedical Imaging and Bioengineering

ONC Certification and Testing Overview

Thomas Keane, MD, Office of the National Coordinator for Health Information Technology

Dr. Keane provided an overview of ONC's role in developing standards and certifying that health IT vendors and products meet those standards. ONC and the Office of Inspector General have established regulations governing behaviors one must engage in to function as information sharers. ONC's website provides details on the eight domains and 58 criteria applicable to certification, along with information on the standards for implementation, companion guides, and a testing tool to help health IT organizations ensure their EHRs are conformant. It's important to note that certification can take up to 2 years for product development, coding, and testing. ONC's Certified Health IT Product List currently includes 609 products and 437 vendors. Certified health IT usage increased from less than 20 percent of hospitals and physician's offices in 2010 to nearly 90 percent in 2020.

In addition, ONC is increasing its post-market surveillance, a common practice in drugs and devices, and particularly relevant given ONC's interest in regulating behaviors and ensuring appropriate information sharing.

FDA Recognition and Use of Standards for Regulatory Decision Making

Tieuvi Nguyen, PhD, U.S. Food and Drug Administration

Dr. Nguyen provided an overview of the FDA's role in the development, recognition, and utilization of standards for regulatory decision making. FDA encourages the development and use of high-quality standards fit for regulatory purposes, with standards overseen by the Standards and Conformity Assessment Program (S-CAP). Specialty Task Groups (STGs) within the S-CAP are made up of experts in regulatory policy, engineering, medicine, and science from different offices across FDA. The STGs align with regulated device areas and review applications for standard recognition. FDA currently recognizes approximately 60 ophthalmic standards, to which device manufacturers may declare conformance in premarket submissions. This is voluntary but highly encouraged as claiming conformity with recognized standards can reduce the amount of documentation required for FDA review, saving both expense and time during device development.

Ocular Imaging in NEI-Supported Collaborative Clinical Research Studies

Jimmy Le, ScD, National Eye Institute

Dr. Le provided an overview of complex multisite clinical trials, which are generally funded as a group of grants comprising (1) a study chair to provide clinical and technical leadership, (2) a data coordinating center for methodological and biostatistical expertise and logistical

coordination, and (3) an image reading center for expertise in the infrastructure for creating images. Image reading centers are interested in standardizing high-quality image capture and forming consensus standards of assessment through publication and dissemination in order to maximize the probability of capturing meaningful changes and outcomes or classifying the severity of different diseases.

Achieving this consensus requires collaboration among reading centers, regulatory agencies, and manufacturers to enable the combination and analysis of ocular imaging data collected across participating sites in multicenter studies. The goal of such analysis is to interpret risk over time; thus, researchers at participating sites need to adhere to strict clinical practice guidelines and operating procedures to ensure that the images are collected and graded properly. To maintain quality, reading centers restrict participation to sites using certified devices and photographers or strict protocols.

Discussion

Identifying and Evaluating Conformance

With no DICOM requirement for ocular images in certified EHRs, it is difficult to benchmark conformance. Panelists agreed that many data elements that would be helpful in both clinical research and patient care have been specified and are available in the DICOM structured report but have not yet been widely implemented by device vendors. Dr. Lee noted that inconsistencies between vendor conformance statements and the actual products cause frustration among researchers and other users.

Panelists discussed possibilities for how data could be stored and encoded in the DICOM structured report to facilitate easy transfer for use in research or analyses by AI or other vendors over time. Dr. Lee noted that ensuring images are in the imaging portion of a DICOM file and that every number generated on an encapsulated PDF and put into a DICOM wrapper is a discrete data element would increase a regulatory body's ability to measure conformance.

Creating and Expanding DICOM Standards for Ocular Imaging

Several panelists noted that DICOM contains existing standards that are not being utilized; barriers to implementation are not necessarily the result of a lack or gap in the DICOM standard. Beginning with standards that already exist can enable the field to better understand what is missing or needs to be expanded. The DICOM standard is flexible and the change control process to add missing elements is not especially onerous.

Stable and diverse funding sources, dedicated resources, and agility to adapt to change are necessary for the long-term sustainability of standards for ocular imaging. Dr. Domalpally noted that many reading centers had to create DICOM platforms in order to mitigate the difficulty of navigating the plethora of vendors, graders, and software related to OCTs. Today, image reading centers do not look at images in proprietary formats, only at DICOM files, but maintaining the platform is time-intensive and requires rebuilding every time there is a new machine or version

update. Although new technology such as OCT-A is welcome, a reading center may need to use it for 2 years before it can determine which biomarkers are useful in a DICOM structured report.

Applications From Radiology

The radiology field may be a useful comparison as it used the combined purchasing power of professional societies, major hospital systems, and research institutions to push for industry standards for imaging. Over the past 40-plus years, radiology vendors have moved from proprietary systems and outputs to widespread interoperability. The mammography field has also shown that new technology platforms can be built on top of viewing platforms. Dr. Juluru noted that starting with the strong foundation of a viewing platform that encourages a third party to develop their own tools to be plugged in can help the industry progress and evolve. Opportunity may exist for a large system such as the Department of Veterans Affairs (VA) to influence what is available as a large purchaser in the market while also considering the general agreement among reading centers on the use of approved machines for clinical trials for research purposes. Panelists noted that the economic structure and incentives in ocular imaging are not identical to radiology and that the encouragement of professional societies, big payers, and large purchasers such as VA and Department of Defense have not pushed the industry to conformity yet.

Advantages and Disadvantages of DICOM

Dr. Linda Wedemeyer noted that many of the DICOM standard advantages are best described by the challenges of not using the standard: interoperability is less feasible; shared images are not standards-compliant or may contain incomplete information limiting functionality to enable ML; analysis software may not be able to address images from different devices over time; and reading centers face increased costs due to licensing fees for PACS to connect any instrument from another vendor. A notable advantage of using the standard is reliable patient data association in the metadata, which decreases the patient and data mis-association rate from at least 5 percent to below 1 percent.

Vendor experience illustrates a disadvantage of using the standard. Dr. Lee noted that when Heidelberg struggled to ensure a legacy viewer worked with their new PACS, the solution of embedding the entire old file object as a binary private tag in the DICOM file resulted in the same number of images requiring twice the amount of hard drive storage space. In addition, how the raw data is transferred from the spectrometer to the DICOM file is proprietary information; thus, requests for vendors to share data or measurements to facilitate standardization must be specific and carefully considered to avoid stifling innovation.

Session 5: Panel Discussion—Approaches to Address the Challenges for Imaging Standardization to Improve the Ecosystem of Ocular Imaging

Moderator: Thomas Keane, MD, Office of National Coordinator for Health Information Technology

Academy Ideas for Approaches to Address Challenges for Imaging Standardization to Improve Eco-System of Ocular Imaging

Flora Lum, MD, American Academy of Ophthalmology

In a values statement, AAO underscored the need for standards in digital imaging, which serves the best interests of the ophthalmic community and the patients they serve. These standards enable the ophthalmology field to progress in the realms of electronic workflow, interoperability, and AI systems. The most fundamental benefits to implementing standards are reduction in costs of service delivery and improvements to quality of care and patient safety. Standardization increases the accessibility of digital images and optimizes the use and delivery of resources to provide patient care. AAO highlighted the importance of interoperability, which is based on the commitment among vendors to shared standards. Global standards allow ophthalmologists to trust that devices will not provide data in unusable, proprietary formats.

AAO strongly encourages imaging device and PACS manufacturers to comply with DICOM standards, which confer many benefits. Standardization of imaging data is a critical part of the medical infrastructure because it provides a common platform for enabling communication between physicians and institutions. DICOM standards benefit patients by facilitating more efficient care. DICOM standards allow physicians to benefit from increasing confidence as consumers of imaging products and devices with a clearly defined level of performance. Manufacturers benefit from DICOM standards through a reduction in costs that would otherwise be required to define service needs for their market. International standards also facilitate the interoperability of products in the global marketplace. Overall, payers and patients benefit from more efficient communications and increases in patient safety due to reduction in human error.

In order to promote DICOM adoption, AAO and the Association for Research in Vision and Ophthalmology (ARVO) plan to issue a joint statement synthesizing content from the NEI-FDA-ONC workshop. This statement will articulate next steps for the clinical and research arms of the ophthalmology field to commit to advancement of standards and will be disseminated to government agencies, payers, research organizations, and ophthalmic practices. The statement will promote imaging standards for clinical trials, device acquisition, medical device evaluation, and certification. AAO sees this action as progress toward a collaborative implementation of standards among all stakeholders.

Promoting the Adoption of Ocular Imaging Standards

SriniVas R. Sadda, MD, University of California, Los Angeles

Representing both ARVO and the International Retinal Imaging Society (IntRIS), Dr. Sadda emphasized the need for not only standards, but also a roadmap for implementation. The lack of stakeholder adoption of standards has led to bottlenecks, particularly in the analysis of large

global datasets. Collaborative solutions are required to implement standards, which require the participation of regulatory agencies, industry, consumers, and professional organizations. Professional organizations can lead the way in promoting standards and IntRIS has produced a proposal to implement this approach. The proposal entails professional organizations formulating their own shared standard, which would include the essential components of a data model for ophthalmology and a system of open standards. Adoption of the standards would be a certification of compliance with several elements, including access to raw data, access to computed data, data storage and transport, data tracking, provision of a code base to access data, commitment to interoperability, de-identification, and user access control. For a certification to be achievable, professional societies and consumers would need to recognize organizations that adopt standards. Standards would be developed through continuous dialogue instead of a static certification process.

The proposed certification mechanism would work though the verification of technical requirements, questionnaires, and documentation. These verification criteria would be formulated through meetings of stakeholder groups that include ophthalmic clinicians, researchers, hardware manufacturers, image reading centers, and collaborators, including the WG-09. Professional organizations would facilitate the inventory of ratified standards, identify key stakeholders, and structure consensus meetings. The goal of these meetings would be to produce certification standards by listing requirements for each technology, formulating questionnaires, establishing required documentation, and considering tiered certifications based on the achievability or level of complexity. Certification types could include meeting standards for OCT devices and viewing software, automated perimetry, image viewing and archival software, and research subject databases.

ONC Perspectives

Micky Tripathi, PhD, MPP, Office of National Coordinator for Health Information Technology

DICOM is among the most stable and long-established standards and has resulted in decreased manufacturing costs in radiologic imaging systems and promoted the use of diagnostic imaging. DICOM has also increased interoperability and transmissibility, as well as enabled the upgrade of systems without concern for backward compatibility. As a result of adherence to DICOM standards, all stakeholders in the radiology market have benefited significantly. While proprietary approaches are informed by the desire of various organizations to have their own standards adopted, DICOM is almost 40 years old with a robust, tested, and widely deployed standards framework. Although virtually all ocular imaging device manufacturers claim DICOM compatibility, interoperability has been elusive because their attestation is not accompanied by evaluation, certification, and testing.

ONC recognizes that attestation may work in some areas while other areas require a formal approach to ensure standards are met. The market would benefit from governmental or third-party conformance certification, based on the standards of interoperability. ONC has the authority to regulate stakeholder behavior through the certification of EHR systems as interoperable. For example, FHIR APIs are required to be supported by all EHR vendors that

cover 95 percent of providers, including ambulatory care and hospitals, by the end of 2022. ONC urges information sharing by administering disincentives and penalties for information blocking.

Compliance with standards could be made easier, and a wide variety of policy levers could be employed to promote the sharing of information, reduction of friction, and maintenance of interoperability as a priority. ONC could also lower barriers to standards development, adoption, and conformance through stakeholder input from community organizations and vendors. Efforts are underway among NEI, ONC, and FDA, and likely VA, DoD, the Indian Health Service, and other government agencies to drive interoperability of ocular imaging devices using all available agency mechanisms. The goal is to generate stakeholder buy-in rather than to force policy changes through regulation incentives and penalties.

Promoting compliance to standards presents both challenges and opportunities. In the development of EHR standards, cyclical periods of compliance occur during which stakeholders meet the letter of the law but not its spirit. This approach can lead to the minimum viable compliance problem, which creates challenges and causes the undesirable escalation of increasingly detailed regulation. However, the rapid increase in EHR use between 2010 and 2020 demonstrates that market adoption of standards can happen quickly, which presents opportunities for progress. This shift bodes well for the accelerated adoption of DICOM standards in ocular imaging.

Addressing the Challenges of DICOM Adoption to Improve the Ocular Imaging Ecosystem

Malvina Eydelman, MD, U.S. Food and Drug Administration

FDA is dedicated to ensuring the safety and efficacy of medical products and aims to advance public health by helping to accelerate innovation. In addition to its previous recognition of DICOM as the standard in radiology imaging, FDA also recently recognized DICOM as the standard for ocular imaging devices. During this recognition process, Dr. Eydelman's team assessed DICOM's structure and content review practices. FDA noted that DICOM differs from typically recognized ophthalmic standards; to keep up with the pace of innovation, DICOM practices a broad, continuous maintenance process that produces updated standards four to five times per year. The first FDA authorization of a device that can provide a diagnostic screening decision without physician input was for an ophthalmic software device used for diabetes patients. This decision highlighted the essential need for interoperability of ocular imaging devices to continue rapid innovation in AI with access to the U.S. market.

In the ophthalmic imaging field, proprietary image outputs are common. However, in the highly connected world, the lack of ability to easily share health data leads to medical errors, duplicative testing, challenges using data for research, and difficulty assessing the performance of treatments. Advancing interoperability standards improves the field of not only ocular imaging devices, but also AI devices. Interoperability is also important to FDA's five steps delineated in the AI/ML-based SaMD Action Plan, which supports the AI/ML regulatory framework, strengthens the harmonization of Good Machine Learning Practice, fosters a patient-centered approach, develops regulatory science methods, and advances real-world performance pilots.

FDA sees interoperability standards as especially important to the AI/ML framework and encourages ophthalmic developers to act as change agents for adopting DICOM standards. All parties in the ocular imaging system benefit from devices that exchange data and are implemented safely and effectively to enable patient care, research, and performance evaluation.

In order to implement interoperability standards, FDA has formulated a five-point plan. The critical parts of this plan are to (1) engage all stakeholders and consider their viewpoints, (2) increase transparency of conformity assessment of the current standard, (3) identify gaps in the currently recognized DICOM standard for ocular imaging devices and modify and improve the standard, (4) consider organizing a Connectathon, and (5) identify potential avenues for acknowledgment or recognition of manufacturers that adhere to the standard. FDA is committed to identifying and supporting collaborative projects, such as the SHIELD laboratory data harmonization initiative and the Digital Medicine Society sensor integration for secondary use initiative.

DICOM's role in compliance is critical. Manufacturers conform to some parts of the DICOM standard but not all—and full compliance to the relevant ophthalmic sections in DICOM can help these stakeholders enhance interoperability. DICOM's standards consist of 22 parts, which correspond to various aspects of communication and management of medical imaging information. Conformance is related to service object-pair classes, representing services (e.g., storage) and operating on types of objects (e.g., OCT images). Functional and performance requirements are described, as well as limitations of interfaces or uses of devices within interoperable systems. DICOM encourages stakeholders to identify gaps in currently recognized standards to improve them. WG-09 activities publish ophthalmology standards improvements on the DICOM website, and all interested parties can participate as WG-09 voting members. To initiate a new meeting, WG-09 members forward a request to the DICOM secretariat. FDA is currently in the process of becoming a voting member.

In order to foster a collaborative approach to developing compliance standards, Dr. Eydelman encouraged workshop participants to host a Connectathon. Connectivity test marathons offer stakeholders face-to-face testing of product interoperability, encourage vendors to work together to solve problems, allow participants to correct non-conformities, hundreds of transactions can be verified using peer tests and tools, and tests can be recorded and validated by neutral monitors. At the end of the event, successful vendors are registered. Participants in the radiology field have experienced successful results from previous Connectathons; however, alternative avenues of recognition for manufacturers should also be sought.

Observations of Conference Remarks

Michael F. Chiang, MD, National Eye Institute

Dr. Chiang thanked workshop participants and summarized key themes that arose during their conversations. The first theme involved resilience. The research and clinical community have shown commitment and diligence in the workarounds they had developed to address complex

challenges presented by imaging devices, image management systems, and EHRs. These workarounds were demonstrated by several examples, including: (1) building software in-house to read images that they could not otherwise access, (2) reviewing imaging studies on multiple machines in parallel, (3) and reverse engineering image data to conduct analyses.

Another major theme during the workshop was the participants' commitment to safety and quality. Workshop participants saw the potential for medical errors and the need to prevent them as a salient priority. AI offers significant potential to increase safety by enhancing image quality and improving communication. Participants also recognized that although some barriers and challenges to interoperability have persisted for decades, the current mood in the field is collaborative, open-minded, and united by a shared commitment to improving care by implementing ocular imaging standards.

A third prominent theme during the workshop was the need for vendors to clearly understand imaging standards. Dr. Chiang observed that vendors need to know what they are being asked to provide, which is not always clear. Different stakeholders have varying means of communicating their needs, which are not always translated well. In turn, vendors should be encouraged to proactively inquire about and attend to requirements. Participants noted that all stakeholders can improve their understanding of the specific needs of their peers. For example, researchers require deidentified data and batch exports, while clinicians need to be able to look at the data for one patient at a time.

Finally, the workshop confirmed participants' desire for more collaborative opportunities. From Connectathons and IHE showcases to reactivating WG-09, participants were enthusiastic about increasing venues to communicate and share information. Connectathons have a track record of success in the pathology and radiology fields (but have had less success when used in the ophthalmology field), and WG-09 made significant progress during its 20 years of activity. The meaningful use of EHRs over the past decade demonstrates that stakeholders are willing to comply with the spirit of regulatory standards, not just adhere to minimum requirements. Regulators can develop more standards, but community buy-in has the best track record for success.

Discussion

Approaches to Incentivizing and Enforcing Ocular Imaging Standards

Paths to Coordinating Market Demand

Given the significant cost of compliance for device manufacturers and vendors, promoting ocular imaging standards requires development of clear and appropriate incentives, which could take the form of certification, regulation, or market demand. Dr. Sadda noted that consumer demand for devices that meet specific standards can motivate compliance by making standardization a competitive advantage.

Dr. Tripathi emphasized that although ONC cannot mandate certification, voluntary certification programs can successfully motivate standards adoption, particularly when multiple stakeholders across the market collectively convey clear demand signals. ONC can coordinate those signals by working with federal partners including FDA and CMS. For example, ONC EHR certification is voluntary, but if CMS requires that ophthalmologists use a certified EHR system in order to participate in its payment programs, that requirement generates a demand signal that travels through the market to impact both consumer and vendor actions.

Dr. Eydelman noted that although utilization of consensus standards is voluntary, complying with FDA-recognized consensus standards can accelerate the process of obtaining FDA approval to bring a device to market. FDA participation in the development or revision of particular standards also results in more frequent use of those standards in device approval applications. Thus, FDA's recognition of DICOM and commitment to provide a liaison should WG-09 reconvene can encourage increased adoption of the standard in the absence of direct regulatory enforcement.

PACS Standardization Challenges

Dr. Chiang noted that the function of PACS in ophthalmology is comparable to that of EHRs in the wider medical field, and clinicians often use PACS and EHRs in parallel. However, PACS are not subject to ONC standards and certifications that apply to EHRs, largely because other entities have regulatory authority over PACS. Dr. Tripathi noted that ONC does offer individual health IT certification modules for specific functions. These standalone modules can apply to systems, such as PACS, that are not traditional EHRs but interact with EHR data inputs and outputs.

Advancing Ocular Imaging Standards through Research Funding

Dr. Chiang emphasized that NEI's role is to create an infrastructure to support research that ultimately improves vision health in the United States. A lack of uniform standards presents a barrier to conducting the most effective research for the benefit of patients and the entire ophthalmological community. Thus, NEI and other organizations that fund research and quality improvement work can best serve their goals by funding research that is poised to leverage an infrastructure for data sharing.

Role of Professional Societies

Professional societies such as AAO and ARVO have strong connections to their membership and the vendor community that they can leverage to educate and engage stakeholders to advance ocular imaging standards adoption. Dr. Lum noted that professional societies can collaborate with each other and with federal agencies to support this goal.
AAO has provided its membership with request for proposal templates that specify the DICOM standard. However, Dr. Wedemeyer noted that enforcing voluntary standards when vendors do not fulfill meet the standards outlined in DICOM conformance statements presents challenges.

WG-09 and Next Steps

Establishing milestones and achievable timelines for next steps in advancing ocular imaging standards requires further discussion among stakeholders. Dr. Sadda noted that reconvening WG-09 could provide a forum in which to determine priority deliverables, inventory gaps in vendors' implementation of standards, and update the current DICOM standard to ensure it reflects current technology. AAO supported WG-09 previously and remains listed as the official secretariat. Dr. Lum noted that AAO would be well positioned to resume secretariat duties and is willing to consider doing so given sufficient interest in the group throughout the ophthalmologic community. However, AAO's previous support of WG-09 concluded due to dwindling vendor participation and financial support. Reconvening WG-09 requires understanding the factors that undermined success previously and a shift in approach to ensure a reinvestment in WG-09 will have meaningful impact. Dr. Eydelman noted that interested stakeholders should sign up as observers or participants on the DICOM WG-09 web page and submit recommendations to DICOM in order to prompt the group to reconvene.

Dr. Tripathi emphasized the importance of developing timelines and funding incentives to motivate action in standards implementation. Participants agreed that concrete milestones are needed to renew interest among stakeholders and drive progress. Dr. Eydelman suggested that a staggered approach that works toward broader goals through multiple stages, deliverables, and milestones can improve the likelihood of success.

Closing Comments

Michael F. Chiang, MD, Director, National Eye Institute

Dr. Chiang closed the workshop by acknowledging the need to engage stakeholders further to develop timelines for advancing ocular imaging standards that consider the need for both incentives and urgency. NEI, FDA, and ONC are committed to collaboratively using their leverage to effect real-world interoperability in the ophthalmological community. This workshop represents an important step toward that goal and its findings will be synthesized and disseminated through a white paper in order to further engage stakeholders.

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