Editorial | Uncover This Tech Term

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Uncover This Tech Term: Independent Central Image Reading

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Independent central image reading (ICIR) refers to the process of objectively reading medical images without knowledge of the patient's personal information, clinical data, or the reading results of other readers (other independent image readers, adjudicators, or researchers from that site) (Table 1). It aims to minimize bias in image interpretation. Initially, the term was coined to describe image interpretation as an endpoint in clinical trials, particularly those aimed at regulatory approval. However, it has since been adopted in various studies in a more general sense, diverging from its specific technical definition to encompass broader meanings. Since 2018, the ICIR has served as the primary or secondary endpoints for efficacy in clinical trials of new anticancer drugs, seeking approval from the United States Food and Drug Administration [1,2], and its scope has gradually expanded. This article aims to explain the meaning of ICIR and related terms within their original technical contexts.

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ICIR is used interchangeably with various terms, such as centralized image interpretation, independent central image review, central reading, and blinded independent central review, but the underlying meanings are similar. ICIR can significantly enhance the reliability of image analysis and ensure consistent results [3]. The extent of clinical data blinding from readers depends on the role of the images in the clinical trial, the nature of the disease, the clinical trial execution process, and investigational drug characteristics (e.g., toxicity). In a randomized controlled trial, biases may occur if the readers interpreting the primary endpoint images have information about the treatment group assignment and access to the clinical information of the trial subjects. Therefore, the readers should be blinded to any related information.

ICIR is performed in a centralized imaging core laboratory. The reading location also referred to as the central imaging center, centralized facility, central imaging laboratory, or central imaging core laboratory, is responsible for designing the necessary imaging protocols for clinical trials as well as collecting and managing the imaging data. Additionally, it verifies the collected images' quality, ensuring consistent and standardized image collection. Compared to the site-based image reading in multicenter clinical trials, the ICIR process allows validation and high-quality reading results through standardized reader training and continuous management to keep readers focused on their readings. Moreover, it minimizes variations in the image reading results and enable accurate treatment efficacy assessment.

The term 'reader' is also used interchangeably with 'reviewer.' The number of individuals participating in a reading depends on the clinical trial design and drug characteristics; however, it typically involves at least three readers [2]: two primary independent readers and one

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Table 1. Terms related to independent central image reading

Term	Definition
Independent central image reading	A process of reading images independently without being influenced by external factors, and in most cases, blinding is used.
Blinded independent central review (BICR)	A type of methodology that is used to evaluate medical images and data in clinical trials objectively.
Centralized imaging core laboratory	An institution responsible for collecting and managing the required images for a clinical trial as well as conducting independent central image reading.
Reader	A person who reads the images compiled at the clinical trial site or centralized image core laboratory.
Adjudicator	A final reader who adjudicates the discrepancies in the assessments of the image readings between readers and confirms cases of disagreement to proceed with re-review.
Clinical trials image management system (CTIMS)	A system used to manage the images utilized in clinical trials.
Imaging case report form (iCRF)	The documents used to record the data related to the images collected in a clinical trial.
Imaging charter	A document describing the contents related to standard techniques and methodologies for image processing required for each clinical trial.
Imaging endpoint	Variables that have clinical relevance to imaging and are directly related to the primary objectives of the clinical trial.
Mock image training	Autonomously implemented training and example readings for the independent reader before the real reading.
Re-read (or re-review)	The procedure for requesting additional readings, reevaluation, and revisions at reconciliation or after receiving data monitoring results.

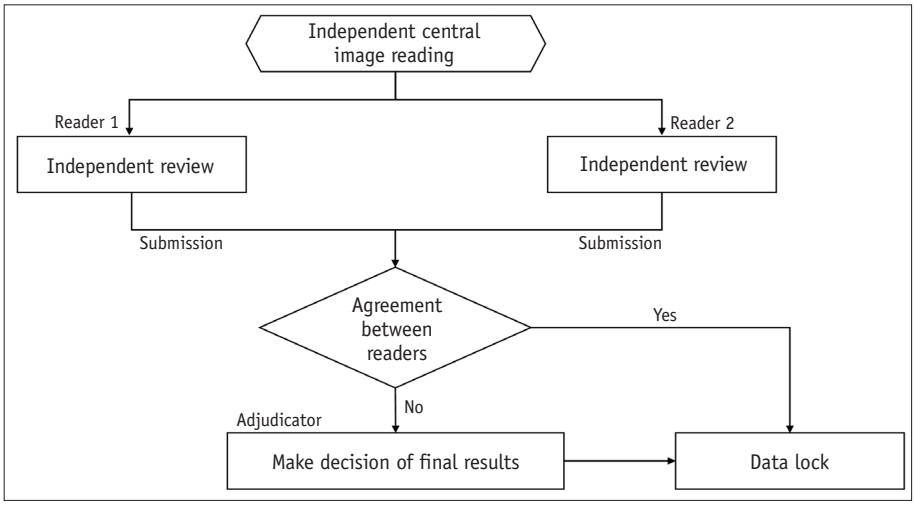

Fig. 1. Independent central image reading process. Independent central image reading typically involves at least two primary independent readers and one adjudicator.

adjudicator. The adjudicator is the final reader who amends the differences and discrepancies in opinions between the primary readers, reconciles any discrepancies, and proceeds with re-reads. The adjudicator is often referred to as the 'moderator' in the context of their role in reconciling differing opinions among primary readers and ensuring consistent and reliable assessments. ICIR typically proceeds according to the procedure shown in Figure 1.

An imaging charter is a document or document series describing the methodology of imaging use, such as procedures for image acquisition, reading, and storage. It should thoroughly describe the strategies to control potential biases and variations in the images and implement standard image processing procedures at appropriate levels for the study design. This document is usually attached as an appendix or included as part of the clinical trial protocol.

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In addition, it comprises or includes methodological summaries of various imaging-related documents such as imaging acquisition plans, data transfer plans, and imaging transmission guidelines for each documented item. These documents contain comprehensive information on the acquisition, transfer, storage, and reading procedures required for imaging in clinical trials. The imaging charter ensures the quality and reliability of the imaging data and guides the accurate analysis and interpretation of the clinical trial results.

An imaging endpoint is an image-driven variable directly related to the main objectives of a clinical trial. The use of medical imaging in clinical trials is progressively increasing; in the anticancer treatment field, progression-free survival (PFS), overall survival, and tumor response based on response evaluation criteria in solid tumours (RECIST) version 1.1 are commonly used imaging endpoints [4].

An example of ICIR serving as the primary endpoint for efficacy is the previous study, in which the PFS of patients with metastatic biliary tract cancer was assessed using the ICIR [5]. The centralized imaging core laboratory Asan Image Metrics (https://aim-aicro.com/en) was responsible for developing imaging protocols, collecting and storing images, and managing blinded ICIR. Two sets of results were derived in this study through ICIR and site investigator reviews. Although PFS and objective response between the two evaluation methods differed slightly, both assessments showed a statistically significant improvement with the study drug, and the hazard ratios yielded similar results in both assessment methods.

With the diversifying ICIR applications, the corresponding need for various types of images, evaluation procedures, criteria, and appropriate standardization arise. ICIR can be valuable not only for facilitating the measurement of image-based evaluation variables but also for assisting in the quality management of images. Specialized reader training for image reading is essential for successful ICIR and must be conducted to meet all requirements.

Conflicts of Interest

Chong Hyun Suh, Assistant to the Editor of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. All authors have declared no conflicts of interest.

Author Contributions

Conceptualization: Sang Eun Won, Sinae Kim, Chong Hyun Suh, Kyung Won Kim. Investigation: Sang Eun Won, Sinae Kim, Chong Hyun Suh. Project administration: Chong Hyun Suh, Hyo Jung Park, Kyung Won Kim. Resources: Chong Hyun Suh, Kyung Won Kim. Supervision: Chong Hyun Suh, Kyung Won Kim. Visualization: Sang Eun Won, Sinae Kim, Chong Hyun Suh. Writing—original draft: Sang Eun Won, Sinae Kim, Chong Hyun Suh. Writing—review & editing: Hyo Jung Park, Kyung Won Kim.

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