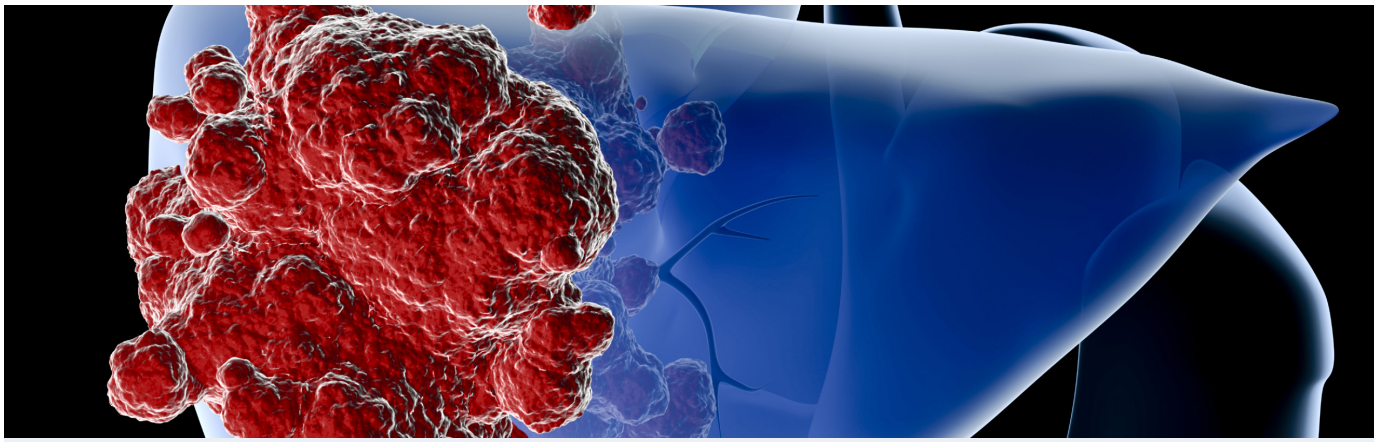
Intrinsic Imaging
www.IntrinsicImaging.com

Guidance for Sponsors
Volume 6, Issue 3 · 2026 Edition

Imaging and Monitoring Tumor Response in Clinical Trials

By Ashwin Shetty, M.D., Radiologist · Updated for 2026 by Intrinsic Imaging



Imaging is the way most cancer trials measure whether a drug works. Objective response rate, progression-free survival and duration of response all depend on images acquired at protocol-defined intervals and interpreted by consistent rules. Over the past fifteen years those rules have multiplied: RECIST 1.1 remains the default, but immunotherapy, molecularly targeted agents, locoregional therapies and PET have each produced their own criteria. This issue explains the current landscape of response assessment and what sponsors must build into a protocol to make imaging endpoints hold up to regulatory review.

Why Response Criteria Exist

Before standardized criteria, response was assessed by individual investigators using their own thresholds, and results could not be compared between trials. The World Health Organization criteria of 1981 introduced bidimensional measurement; RECIST in 2000 simplified it to a single longest diameter; and RECIST 1.1 in 2009 fixed the number of target lesions at five (two per organ), defined lymph node measurement on the short axis and clarified how progression is declared.[1] RECIST 1.1 remains the standard that the FDA expects for solid tumor trials unless there is a scientific reason to use something else.[2]

Criteria for New Mechanisms of Action

Immune checkpoint inhibitors can produce 'pseudoprogression', an apparent increase in tumor burden or new lesions followed by durable response. iRECIST, published by the RECIST Working Group in 2017, introduced the category of unconfirmed progression (iUPD) that must be confirmed on a subsequent scan four to eight weeks later before a patient is declared to have progressed.[3] For lymphoma, the Lugano classification of 2014 replaced the older Cheson criteria, made FDG-PET with the Deauville five-point scale the standard for FDG-avid lymphomas and eliminated the category of complete response unconfirmed.[4] For hepatocellular carcinoma treated with locoregional or antiangiogenic therapy, mRECIST measures only the enhancing viable tumor; the criteria were updated in 2020 to clarify their use in systemic therapy trials.[5] The LI-RADS Treatment Response Algorithm, revised in 2024, now distinguishes assessment after radiation-based from nonradiation locoregional therapy.[6]

Molecular imaging has its own framework. PERCIST uses standardized uptake values corrected for lean body mass to define metabolic response on FDG-PET, and is widely used as a secondary endpoint and in trials where anatomic size changes slowly.[7] Targeted PET tracers such as PSMA agents for prostate cancer have created new opportunities to detect disease earlier and to select patients for radioligand therapy, although anatomic criteria still govern most regulatory endpoints.

Toward Volumetric and Quantitative Imaging

A single diameter is a crude measure of a three-dimensional, often irregular tumor. Volumetric segmentation is more sensitive to change and less variable between readers, and the RECIST Working Group has stated that volumetric assessment is under active evaluation as part of future revisions to the criteria.[8] The Quantitative Imaging Biomarkers Alliance has published profiles for CT tumor volume, FDG-PET SUV and diffusion-weighted MRI that specify how to acquire and process images so that measured change reflects biology rather than technique.[9] Sponsors who want volumetric or functional endpoints should adopt these profiles and discuss their use with regulators before the trial begins.

What Regulators Expect

The FDA's 2018 guidance on clinical trial imaging endpoint process standards describes what a sponsor should document when imaging supports a primary or key secondary endpoint: a standardized acquisition protocol, site qualification, an imaging charter that specifies the read paradigm, reader training and qualification, blinded independent central review (BICR) and quality control of images and reads.[2] BICR, with two independent readers and adjudication, is expected when the trial is open-label or when progression-free survival is the primary endpoint, because investigator assessment is subject to bias. Discordance between local and central reads of 20 to 40 percent is common, and the central read is the one that supports the label claim.

Practical Pitfalls

The most frequent problems in imaging endpoints are mundane. Target lesions selected at baseline that are not truly measurable; slice thickness that varies between visits; contrast timing that differs from one scan to the next; lesions that are measured on different sequences at different timepoints; and scans acquired outside the protocol window. Each introduces noise that is indistinguishable from treatment effect. A well-run core lab prevents these errors at the point of acquisition by qualifying sites before enrollment, reviewing every scan on receipt and querying deviations immediately rather than at database lock.

Guidance for Sponsors

Imaging endpoints in oncology trials

- **Choose criteria that fit the mechanism.** RECIST 1.1 by default; iRECIST for immunotherapy; Lugano for lymphoma; mRECIST or LI-RADS TR for HCC and locoregional therapy.[1,3,4,5,6]
- **Write an imaging charter.** Define acquisition, read paradigm, reader rules and adjudication before the first patient is scanned.[2]
- **Use blinded independent central review.** Especially for open-label trials and PFS endpoints.[2]
- **Standardize acquisition.** Fixed slice thickness, contrast phase and scan windows across all sites and visits.[9]
- **Consider quantitative add-ons.** Volumetrics, PERCIST or DWI as exploratory endpoints following QIBA profiles.[7,8,9]
- **Qualify sites and query early.** Review images on receipt so protocol deviations do not accumulate.

Summary

Response criteria are the language in which oncology trials report their results, and the language has grown richer. Choosing the right criteria, documenting the imaging process to regulatory standards and reading centrally are what turn images into evidence. Sponsors who invest in that infrastructure early avoid the costly surprises that imaging endpoints can otherwise produce at the end of a trial.

About the Author

Dr. Ashwin Shetty, a radiologist at Intrinsic Imaging, wrote the original edition of this issue. He completed his residency in diagnostic radiology and fellowship training in body imaging, and he interprets oncologic CT, MRI and PET across a wide range of solid tumors. He is board-certified in diagnostic radiology.

References

1. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45(2):228–247. doi.org/10.1016/j.ejca.2008.10.026

2. U.S. FDA. Clinical trial imaging endpoint process standards: guidance for industry. April 2018. fda.gov

3. Seymour L, Bogaerts J, Perrone A, et al. iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics. *Lancet Oncol.* 2017;18(3):e143–e152. doi.org/10.1016/S1470-2045(17)30074-8

4. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol.* 2014;32(27):3059–3068. doi.org/10.1200/JCO.2013.54.8800

5. Llovet JM, Lencioni R. mRECIST for HCC: performance and novel refinements. *J Hepatol.* 2020;72(2):288–306. doi.org/10.1016/j.jhep.2019.09.026

6. Fowler KJ, Burgoyne A, Fraum TJ, et al. LI-RADS treatment response algorithm version 2024. *Radiology.* 2024;313(2):e232408. pubmed.ncbi.nlm.nih.gov/39535775

7. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. *J Nucl Med.* 2009;50(Suppl 1):122S–150S. doi.org/10.2967/jnumed.108.057307

8. RECIST Working Group, EORTC. RECIST: Response Evaluation Criteria in Solid Tumours. recist.eortc.org

9. Radiological Society of North America. Quantitative Imaging Biomarkers Alliance (QIBA) profiles. qibawiki.rsna.org

About Intrinsic Imaging, LLC

Intrinsic Imaging is an ISO certified medical imaging CRO and imaging core lab providing comprehensive services in support of Phase I-IV clinical trials and Class I, II, III medical device trials. Intrinsic Imaging is also a world leader in conducting Artificial Intelligence studies. With its team of more than 650 board-certified and fellowship-trained physicians, Intrinsic Imaging's team has sub-specialization in all therapeutic areas, including Cardiovascular, Central Nervous System,Gastroenterology, Musculoskeletal, Oncology and Ophthalmology. Certified by the British Standards Institution (BSI), Intrinsic Imaging is the only company in the world to hold five ISO certifications specifically for providing imaging core lab services on clinical trials. For more information, please visit www.IntrinsicImaging.com.

Contact

Intrinsic Imaging, LLC
580 Main Street, Suite 210
Bolton, MA 01740
Tel: +1 978-616-4650
Contact@IntrinsicImaging.com
www.IntrinsicImaging.com