Using Choi Criteria in Oncology Clinical Trials

Imaging Endpoints – Connecting Imaging to the Cure

Choi criteria can provide a window into anti-tumor activity when traditional methods fail to reveal response outcomes that are demonstrated in improved patient outcomes. It is not uncommon that targeted therapy and precision medicine do not alter tumor size but do alter the appearance of tumors. Traditional response criteria such as RECIST 1.1 focus on changes in the size of lesions to evaluate a response outcome. Choi criteria focuses on changes in tumor enhancement (density) on CT as an indicator of response that may be observed with or without evidence of size changes in lesions on imaging.

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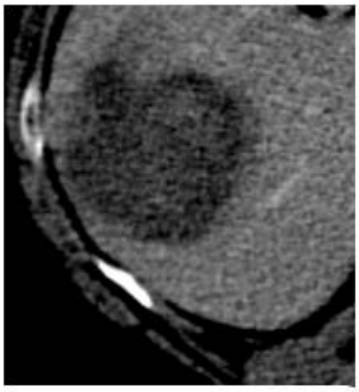
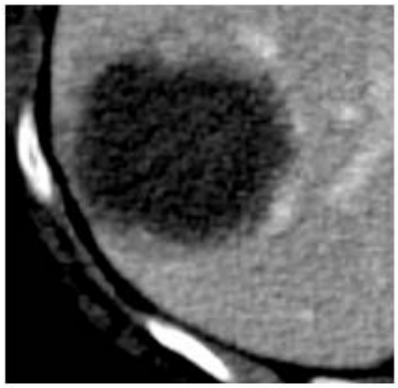
Why use Choi Criteria?

In landmark publication in 2007, Choi[1] and colleagues found that in evaluating response in GIST subjects, significant changes in tumor density, enhancing intratumoral tumor nodules and tumor vessels on CT imaging were observed after treatment with imatinib. Tumor density measured as CT attenuation coefficient (Hounsfield unit [HU]) in conjunction with less dramatic size changes in lesions were found to provide a robust method to evaluate treatment response. A decrease in density observed in lesions on CT correlated with tumor necrosis or cystic or myxoid degeneration in these lesions.



Baseline Density= 59.0 HU

Baseline Diameter= 49.2 mm



Follow-Up Density= 41.3 HU

Follow-Up Diameter= 49.2 mm

Two disadvantages of density measurements, however, include not being applicable to MRI and a lack of validation or usefulness in pulmonary lesions. For this reason, in lesion selection at baseline, lung lesions are typically followed as Non-Target lesions. Additionally, for accurate determination of treatment response, only CT scans can be utilized to assess the response.

Just as traditional size-based response criteria may not correlate actual patient outcomes, Choi criteria may not be suitable for all tumor types and all therapies. Careful analysis of the early Phase I data can, however, help to determine the best response criteria to evaluate a given therapy's potential anti-tumor response.

Choi criteria would provide particularly useful in GIST and may be useful in Hepatocellular Carcinoma, and Renal Cell Carcinoma and some other solid tumors.

Implementing Choi Criteria in Radiological Evaluation of Response

Choi criteria utilizes general lesion selection and size-based response according to RECIST 1.0. Density evaluation is performed using the CTattenuation coefficient (density) of each tumor in HU by drawing a region of interest (ROI) around the entire measured lesion. All disease is catalogued into 2 compartments at baseline following the guidelines of RECIST 1.0: Target Lesions and Non-Target Lesions. Using a composite assessment of size criteria and density changes for Target lesions, in conjunction with non-target disease, and the appearance of new lesions at follow-up, an overall response is derived. Unlike traditional RECIST however, an increase in tumor size that meets a defined PD (≥ 10%) is not an automatic trigger for progression if a decrease in tumor density of ≥ 15% is observed on CT.

[1]Choi H, Charnsangavej C, Faria SC, et al. Correlation of computed tomography and positron emission tomography in patients with metastatic gastrointestinal stromal tumor treated at a single institution with imatinib mesylate: proposal of new computed tomography response criteria. J Clin Oncol. 2007; 25:1753–1759.

Overall Time Point Response

	Target Lesions	Non-Target Lesions	New Lesions
Complete Response (CR)	CR	CR or None at BL	None
	None at BL	CR	None
Partial Response (PR)	PR	CR, IR/SD or None at BL	None
	CR	IR/SD	None
Stable Disease (SD)	SD	No PD or None at BL	None
	None at BL	IR/SD	None
Progressive Disease (PD)	Target or Non-Target Lesion Progression **and/or** New Lesion appearance **NOTE**: Target Lesions must not demonstrate PR by density (HU)		
Not Evaluable (NE)	At least one Target Lesion or Non-Target Lesion is not evaluable and no progression is otherwise observed.		

Baseline Evaluation

Measurable Disease – Target Lesions

- Target Lesions are measured in longest diameter unidimensionally
- Up to 10 Target lesions with no more than 5 lesions per organ are identified at baseline.
- Target Lesions may include Nodal and Non-Nodal sites.

Target Lesions	Lesions **≥ 10 mm in longest diameter** (or 2x Slice Thickness if slice thickness is > 5 mm) **Measurement**: Uni-dimensional ruler measurement of the longest diameter Includes nodal and non-nodal sites; Nodal sites should be pathological

Non-Measurable Disease – Non-Target Lesions

- Non-Target Lesions are followed qualitatively at baseline.
- Non-Target lesions include:
  - Measurable lesions in excess of 10 Target lesions
  - Lesions smaller than the criteria for Target lesions but abnormal and consistent with disease
  - Lung lesions, Bone lesions, Leptomeningeal disease, Ascites, Pleural/pericardial effusions, Lymphangitis cutis/pulmonis, Inflammatory breast disease

Follow-up Evaluation

Target Lesions

- Target Lesions are re-measured at follow-up and the Target lesion SLD is compared to baseline and nadir to determine response/progression status.
- Decreases in tumor burden must be assessed relative to baseline measurements. Increases in tumor burden are assessed relative to nadir.

Target Lesions	
Complete Response (CR)	Disappearance of all Target Lesions. No pathological lymph nodes.
Partial Response (PR)	A decrease in size of ≥10% **OR** A decrease in tumor density (HU) ≥15% on CT
Stable Disease (SD)	Does not meet the criteria for CR, PR, or PD
Progressive Disease (PD)	An increase in tumor size of ≥10% **AND** Does not meet criteria of PR by tumor density (HU) on CT
Not-Evaluable (NE)	Progression has not been documented and one or more Target lesions have not been assessed or have been assessed using a different method than baseline that makes comparability impossible.

Non-Target Lesions

- Non-Target Lesions are followed qualitatively at follow-up time points.
- All Non-Target lesions should be evaluated visually at each time point, and examined for presence or absence and for evidence of unequivocal progression of individual lesions as well as of the overall Target lesions.

Non-Target Lesions	
Complete Response (CR)	Disappearance of all Non-Target lesions. No pathological lymph nodes.
Incomplete Response/ Stable Disease (IR/SD)	Persistence of one or more Non-Target lesion(s)
Progressive Disease (PD)	Unequivocal progression of Non-Target lesions
Not-Evaluable (NE)	No progression and one or more Non-Target lesions have not been assessed

New Lesions

- Unequivocal new lesions reported as follow-up.
- There is no minimum size for a new lesion. New nodal lesions should be pathological.
- A lesion identified on a follow-up study in an anatomical location that was not scanned at baseline is considered a new lesion.
- New lesions may include new intratumoral nodules.

Other Considerations - Using Choi Criteria with RECIST 1.1

A modification of Choi may be implemented using RECIST 1.1 Guidelines. Modifications would include:

- ✓ Up to 5 Target Lesion at BL (no more than 2 per organ) with Nodal Lesions measured in short axis and Non-Nodal lesions measured in long axis.
- ✓ Minimum Target Nodal size: ≥ 1.5 cm in short axis. Nodes ≥1.0 cm in short axis are considered pathological and followed as Non-Target if they do not meet size criteria for Target lesion selection.
- ✓ Subjects with no Target lesions who do not achieve a CR would have an overall response of Non-CR/Non-PD if no progression observed rather than SD.
- ✓ Not Evaluable Non-Target lesions would prevent CR but would not drive an overall assessment of NE.
- ✓ Tumor density evaluation as originally described in Choi criteria for PR and PD would be implemented along with unique size criteria and percentage changes based on Sum of Diameters.