Advancing QIBA Profiles to “Claim Confirmed” Stage: FDG-PET/CT Example

Profile Stages

Stage 0: Selected
- submit and approve proposal

Stage 1: Public Comment
- draft profile and publish

Stage 2: Consensus
- review/revise after public comments

Stage 3: Technically Confirmed
- evaluate how profile procedures work in field and revise

Stage 4: Claim Confirmed
- validate statistical assumptions in the field and revise

Stage 5: ClinicallyConfirmed
Stage 4: Claim Confirmed

• Key Purpose:
  • evaluate validity of statistical assumptions underlying claims
  • confirm that actual performance at a real site is consistent with performance in claims

FDG-PET/CT Profile Claims

• Claim 1: Tumor glycolytic activity as reflected by the maximum standardized uptake value ($\text{SUV}_{\text{MAX}}$) is measurable from FDG-PET/CT with a within-subject coefficient of variation of 10 -12%.

• Claim 2: A measured increase in $\text{SUV}_{\text{MAX}}$ of 39% or more, or a decrease of -28% or more, indicates that a true change has occurred with 95% confidence.
FDG-PET/CT “Claim Confirmed” Study

• **Primary objective**: To measure test-retest repeatability of FDG uptake (SUVmax) in human solid tumors and assess effects of FDG uptake intensity, lesion diameter and location on test-retest repeatability.

• **Secondary objectives**:
  • Estimate effect of point spread function modeling.
  • Estimate test-retest reader and interpretation system reproducibility
  • Measure test-retest repeatability of FDG SUV$_{PEAK}$

FDG-PET Proposed Study

• Multi-center, single arm design (5-10 sites proposed)

• Subjects with pathologically proven solid tumor or lymphoma with at least one target lesion with SUVmax > 4 and greater than 2 cm in longest diameter.

• Subjects recruited based on site of primary tumor, with equal representation of lung cancer, head/neck cancer, lymphoma, breast cancer, and “other”.
FDG-PET Proposed Study

Standard of care FDG-PET/CT scan following QIBA profile

Meet claim requirements and no change in therapy?

no → Not considered

yes → Repeat FDG-PET/CT scan within 1-7 days with same scanner

Sample Size Assumptions:

• Mean wCV over all clinical sites is 10%
• wCV varies between sites with a range of 8% to 12%
• Within a site, ground truth SUV\textsubscript{MAX} values have a between-subject standard deviation of 6.0. (Literature data)
• Each site contributes same number of subjects (balanced design)
• Subjects have 2 measurable lesions (5 lesions allowed per subject)
Predicted 95% CIs based on model assumptions (5 sites assumed)

<table>
<thead>
<tr>
<th>Total # Subjects</th>
<th>75</th>
<th>100</th>
<th>125</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>#/site</td>
<td>15</td>
<td>20</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Predicted estimation of 95% CI around mean wCV</td>
<td>[7.8, 12.8]</td>
<td>[8.1, 12.4]</td>
<td>[8.2, 12.1]</td>
<td>[8.5, 12.0]</td>
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After taking into account 10 incomplete scans/drop outs, and 10 scans not performed correctly, 120 subjects would be needed to yield 100 complete and analyzable test-retest scans.

Status of Proposed Study

- Submitted to ECOG-ACRIN
- Reviewed by Imaging Science Advisory Committee on April 17
- ISAC voted to “Recommend” proposal
- Proposal revised and submitted to Executive Committee on May 2
- Executive Committee will review proposal on May 24