Clinical Trials Assessing Imaging Tools in Cancer Management

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Imaging Tools For Cancer Management

- screening
- diagnosis
- staging
- stratifying patients based on biologic characteristics of the primary tumor and metastases
- guiding therapeutic interventions
- assessing therapeutic response
- surveillance
Evaluating patients based on biologic characteristics of the primary tumor and metastases for personalized care

- Prognostic Markers
- Predictive Markers
- Assessing therapeutic response
- Focused surveillance/screening
Molecular and Functional Imaging

Key issues in imaging tool assessment:

- Preliminary efficacy
- Reproducibility
- Tissue correlation

In the context of patient management with standard treatment:
- prognostic capabilities
- predictive capabilities
- assessment of treatment response
Standardization

Issues:

- Variability of signal –
  - Within a histology
  - Within a patient on different days (without therapeutic intervention)
  - With different scanners from the same manufacturer
  - With scanners from different manufacturers
  - With different therapeutic interventions
Clinical Trial Networks in the Division of Cancer Treatment and Diagnosis

- Experimental Therapeutics Clinical Trials Network (ETCTN)
- NCI National Clinical Trials Network (NCTN)
- Pediatric Brain Tumor Consortium (PBTC)
- Adult Brain Tumor Consortium (ABTC)
- Pediatric Early Phase Clinical Trials Network (PEP CTN)
ETCTN

ETCTN Sites

NIH NATIONAL CANCER INSTITUTE
NCTN

NCI National Clinical Trials Network Structure

LEGEND

- Centralized Functions:
  - Centralized Institutional Review Board
  - Cancer Trials Support Unit
  - Imaging and Radiation Oncology Core (IROC) Group
  - Common Data Management System Central Hosting

- 30 Lead Academic Participating Sites (LAPS)
- Operations
- Statistics & Data Management
- Tissue Banks
- Member Sites
Resources for Imaging and RT Activities within the ETCTN and NCTN

For efficient assessment of promising imaging agents and modalities and their role in the development of therapeutic strategies and cancer management:

- Development of a national distribution system for investigational imaging agents
- Biomarker, imaging, and quality of life studies funding program (BIQSFP)
- Imaging and Radiation Therapy Core (IROC) for the NCTN
- Clinical Imaging and Disease Specific Steering Committees
- PAs and PARs
Diagnosis and Staging
Multiparametric prostate MRI

Figure 3. Advantage of small field-of-view (FOV) DWI. 66 year-old patient with PSA 6.1. 351 ng/ml. A: T2WI shows a lesion in the right anterior mid transition zone (arrow). Restricted. 352 diffusion is demonstrated with high signal on the b-1400 DWI (B, D) and corresponding low. 353 signal on the ADC maps (C, E), with small FOV imaging showing improved signal-to-noise 354 ratio and increased lesion conspicuity (D, E), compared to standard DWI (B, C).
EA8171: Multiparametric MRI (mpMRI) for Preoperative Staging and Treatment Planning for Newly-Diagnosed Prostate Cancer.

Primary Objectives:

• To estimate the diagnostic performance of overall PI-RADS score based on local site imaging review of mpMRI (T2W, DWI and DCE) to detect clinically significant prostate cancer.

• To develop a risk prediction model by incorporating overall PI-RADS, PSA, Gleason score and clinical stage to predict the presence of clinically significant significant prostate cancer.
18F-DCFBC PET (A) and T2-weighted MR (B) images demonstrating 18F-DCFBC photopenia for representative example of BPH nodules (arrowheads) within central prostate. Steven P. Rowe et al. J Nucl Med 2015;56:1003-1010

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EA8191: Phase III Study of Local or Systemic Therapy INtensification DIdrected in Prostate Cancer Patients with Post-ProstaTEctomy Biochemical Recurrence (INDICATE).

Primary Objectives:

- For patients without PET-evidence of extrapelvic metastases, to evaluate whether the addition of enhanced systemic therapy to SOC salvage RT could prolong PFS.
- For patients with PET-evidence of extrapelvic metastases, to evaluate whether the addition of metastasis-directed RT to enhanced systemic therapy and SOC salvage RT could prolong PFS.
Theranostics:

- $^{177}$Lu-PSMA radioligand therapy in a 67-year-old man with metastatic castration-resistant prostate cancer.

- **a** Pretherapy. PET image evidenced a diffuse metastatic involvement. PSA value 50 ng/ml.

- **b** 4 months following the treatment with $^{177}$Lu-PSMA radioligand therapy (8000 MBq), PET showed a complete metabolic response. PSA value 0 ng/ml

Predictive Marker
EAI142: $[^{18}\text{F}]$ Fluoroestradiol (FES) PET as a Predictive Measure for Endocrine Therapy in Patients with Newly Diagnosed Metastatic Breast Cancer.

Primary Objective:

• To determine the negative predictive value (NPV) of $[^{18}\text{F}]$Fluoroestradiol (FES) uptake for response (clinical benefit) at 6 months in patients with estrogen-receptor positive (ER+) metastatic breast cancer treated with first-line endocrine therapy.
Pharmacodynamic Marker
Perfusion MRI in treatment evaluation of glioblastomas: Tumor progression
Perfusion MRI in treatment evaluation of glioblastomas: pseudoprogression
EAF151: Change in Relative Cerebral Blood Volume as a Biomarker for Early Response to Bevacizumab in Patients with Recurrent Glioblastoma.

Primary Objective:

• To determine whether the binary change (increase vs. decrease) in normalized rCBV within enhancing tumor from the baseline scan (S0) to the post-dose 1 treatment scan (S1) is associated with overall survival (OS) in recurrent GBM patients receiving bevacizumab or its biosimilars for the first time
Response Assessment
Diffusion Weighted MRI

- Metastatic prostate cancer pre and post systemic therapy

EA2174: A Phase II/III Study of Peri-operative Nivolumab and Ipilimumab in Patients with Locoregional Esophageal and Gastroesophageal Junction Adenocarcinoma.

Primary Objectives:

- To assess the pathCR rate following administration of neoadjuvant carboplatin, paclitaxel and radiation therapy versus neoadjuvant carboplatin, paclitaxel, radiation therapy and nivolumab in patients with a resected locoregionally advanced esophageal or gastroesophageal junction adenocarcinoma.

- To assess the disease-free survival (DFS) following administration of adjuvant nivolumab and ipilimumab versus adjuvant nivolumab in patients with a resected locoregionally advanced esophageal or gastroesophageal junction adenocarcinoma who received neoadjuvant treatment with carboplatin, paclitaxel and radiation therapy with or without nivolumab.
NRG-GI002: A Phase II Clinical Trial Platform of Sensitization Utilizing Total Neoadjuvant Therapy (TNT) in Rectal Cancer.

Primary Objective:

- To demonstrate an absolute improvement in Neoadjuvant Rectal Cancer (NAR) score for the experimental regimen as compared to concurrently randomized control patients.
Metabolic response with residual morphologic lesion (arrows) as seen on PET (top), CT (middle), and PET/CT (bottom) images. Amir Iravani, and Rodney J. Hicks J Nucl Med 2020;61:943-950
Primary Objective:

- To evaluate the performance of FDG-PET/CT response criteria (modified PERCIST complete, partial and stable metabolic disease versus progressive metabolic disease) as a binary predictor of PFS in patients with BD MBC treated with systemic therapy.
Collaborations for Assessment of Imaging Tools

- NCI-FDA (Tracer development pathways)
- NCI-CMS
- NCI-EORTC
- Response Assessment – collaboration with EORTC and Pharma
  - RECIST 1.1
  - FDG – ongoing evaluation
- QIBA
- Biomarkers Consortia
Clinical Trials Branch Staff

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