Quantitative thermal imaging biomarkers to detect acute skin toxicity from breast radiation therapy using supervised machine learning

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**Outcomes**

**Data Acquisition**
- Image Display
- Photon → Electron → Voltage → Digital Signal
- IR Lens → Sensor → Signal Processor → Interface I/O

**Segmentation/Feature Extraction**
- Infrared Image → Skin Rendering → ROI Selection
- 1st Order Features (n=8): μT(°C)
- 2nd Order Features (n=25):
  - GLCM (n=4)
  - GLRLM (n=16)
  - GTDM (n=5)

**Analysis**
- Patient Groups
  - CTCAE ≥2: n=37
  - 1st and 2nd Order Features Averaged
  - T-Test Or Mann-Whitney: Between Group Differences
  - Repeated Measures ANOVA: In-between Group Differences
- CTCAE ≤1: n=53
- Statistical Model (Baseline + All fractions): Verifying differences in temperature and textural features as characteristics of patient’s skin toxicity.

**Outcomes**
- CTCAE ≥2: n=37
  - Initial Feature Set
  - Training Data (n=75)
  - Balancing Data (100 bootstrap samples)
  - Sequential Forward Feature Selection
  - Validation Loop
- CTCAE ≤1: n=53
  - Training Data (n=75)
  - Balancing Data (100 bootstrap samples)
  - Model Training
  - Predictive Model (Validated)
  - Random Forest

**Validation Loop**
- Calculating sensitivity, specificity and AUC for unseen patients in the test set (n=15).
**Ipsilateral**

### Mean Temperature (°C)

**A**

- **CTCAE (≥2)**
- **CTCAE (≤1)**

**B**

- **CTCAE (≥2)**
- **CTCAE (≤1)**

### Contralateral

### Mean Temperature (°C) at 10th Treatment Fraction

- **Ipsilateral**
- **Laterality**
- **Contralateral**

<table>
<thead>
<tr>
<th>Fractions</th>
<th>ΔμTavg</th>
<th>p</th>
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<tr>
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<td>0.302</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>0.199</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>0.302</td>
<td>1</td>
</tr>
</tbody>
</table>

- **p=0.029**
- **p=0.199**

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**Mean Temperature (°C):**

- **CTCAE (≥2):**
  - Baseline: 34.0°C
  - Fractions: 5: 34.5°C (p=0.029)
  - Fractions: 10: 35.0°C (p=0.199)
  - Fractions: 15: 35.5°C (p=0.302)

- **CTCAE (≤1):**
  - Baseline: 36.0°C
  - Fractions: 5: 36.5°C
  - Fractions: 10: 37.0°C
  - Fractions: 15: 37.5°C

**Laterality:**

- **Ipsilateral:**
  - 0.024°C
  - 0.302°C
  - 0.319°C
  - 0.222°C
  - 0.227°C
  - 0.182°C
  - 0.229°C
  - 0.302°C

- **Contralateral:**
  - 0.302°C
  - 0.302°C
  - 0.302°C
  - 0.302°C
  - 0.302°C
  - 0.302°C
  - 0.302°C
  - 0.302°C

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**CTCAE (≥2):**

- Baseline: 34.0°C
- Fractions: 5: 34.5°C (p=0.029)
- Fractions: 10: 35.0°C (p=0.199)
- Fractions: 15: 35.5°C (p=0.302)
Experiment One
Optimal Feature Set:
Max. Temp(°C), Median Temp(°C), Mean Temp(°C), Skewness, Kurtosis

Experiment Three
Optimal Feature Set:
Mean Temp(°C), GLCM-COR, GLCM-ENE, GLCM-HOM, GLRLM-GLN

Receiver operating characteristic

ROC Curve (area = 0.90)

ROC Curve (area = 0.98)
Supplementary Figure A.
Representative images of the skin reaction of the irradiated breast across RT treatment for a patient with an end-of-treatment score of CTCAE≥2 (top) and for a patient with a score of CTCAE≤1 (below). The CTCAE≥2 patient demonstrates noticeable dermatological changes and erythema which is most noticeable starting at the 10th fraction. A temperature scale bar is presented for the thermograms.
Supplementary Figure B

Temperature and first order features of the ipsilateral (irradiated) breast. Statistical significance was found for temperature between the patient groups at the 10th and 15th fractions. There was no statistically significant difference found between our patient groups for any of the first order features.
Supplementary Figure C
Temperature value distribution for GLCM features of the ipsilateral (irradiated) breast. There was no statistically significant difference found between our patient groups for any of the GLCM textural features.
Supplementary Figure D

Temperature value distribution for GLRLM features of the ipsilateral (irradiated) breast that demonstrated good predictive value. There was no statistically significant difference found between our patient groups for any of the GLRLM textural features, except for GLRLM-SRE (10th fraction).
Supplementary Figure E

Temperature value distribution for GTDM features of the ipsilateral (irradiated) breast. There was no statistically significant difference found between our patient groups for any of the GTDM textural features.