A Novel Computer-Aided Diagnostic System for Early Assessment of Hepatocellular Carcinoma

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Research Motivations

6th Leading cancer in the world

1st Rising death cause cancer in the USA

The blue faery liver cancer association 2020
Research Motivations

Annual records:

- Worldwide: 800,000 new cases and 700,000 new deaths
- In the USA: 42,030 new cases and 31,780 deaths

At Global Averages:

1/5000 People is in danger of contracting HCC

The blue faery liver cancer association 2020
HCC is a cancer arising from the liver cells.

HCC is the most common primary liver disease, and its incidence is increasing.

The prognosis of HCC is affected by its severity level when detected, as curative managements can be enough for early-stage HCC.

Early assessment of liver cancer patients with HCC is of immense importance to provide the proper treatment plan.
Current Diagnostic Tools & Limitations

- For **HCC**, a radiological diagnosis (LI-RADS) provides high diagnostic performance and is considered as the **Gold-Standard**, which makes the medical organizations depend only on highly-experienced radiologists for HCC diagnosis.

- Therefore, there is an urgent need for an **automated machine-learning based CAD system** to identify HCC and its grade to provide the proper treatment plan.

Liver Imaging Reporting and Data System (LI-RADS v2018)
Proposed Framework

Input Data:
- Dicom Images
- Binary Masks

2D Extracted Tumor Lesion Slices (ROI)

3D Structure (ROI)

Extracted Features
- Texture Features
  - 1st Order Histogram
  - 2nd Order GLCM
  - 2nd Order GLRLM
- Shape Features
  - Spherical Harmonics
- Functional Features
  - Wash-In
  - Wash-Out

2-Stage Classification using Fusion of Features

Random Forests Classifier

Input: Benign

Pre-Processing: LR-1, LR-2

Features Extraction: LR-3

Classification: LR-4, LR-5
A total of 85 patients with high risk of developing HCC without history of loco-regional treatment plan, (M = 61 and F = 24), provided their consent to participate in this study.

They averaged an age of (55.131 ± 7.12) ranging from 40 to 73 years old.

34 patients with benign tumors (LR-1 = 17 and LR-2 = 17), 17 with intermediate, and 34 with malignant tumors (LR-4 = 17 and LR-5 = 17)

Acquisition parameters of MRI sequences are defined in the following Table:

<table>
<thead>
<tr>
<th>Sequence</th>
<th>TR (msec.)</th>
<th>TE (msec.)</th>
<th>FOV (mm)</th>
<th>Matrix</th>
<th>Slice thickness (mm)</th>
<th>Slice gap (mm)</th>
<th>Flip angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>&gt;=445</td>
<td>26-28</td>
<td>230</td>
<td>160-144×240</td>
<td>6</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>T2 SPAIR</td>
<td>2500-3000</td>
<td>80-100</td>
<td>230</td>
<td>144×144</td>
<td>6</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>Dynamic GRE (THRIVE)</td>
<td>7.3</td>
<td>3.1</td>
<td>500</td>
<td>256×128</td>
<td>3</td>
<td>1</td>
<td>40</td>
</tr>
</tbody>
</table>

Acquisition parameters of MRI sequences. TR: repetition time; TE: echo time; FOV: field of view; SPAIR: spectral attenuated inversion recovery; GRE: gradient-recalled echo; THRIVE: T1-weighted, high-resolution isotropic volume examination.
Liver Tumor Preprocessing
Here, we extracted texture analysis features from the gray-level histogram of the four 3D constructed objects for each tumor lesion.

The computed features are mean, variance, standard deviation, skewness, kurtosis, entropy, cumulative distribution function and gray-level percentiles.
Features Extraction: Texture Features (cont’d)

2nd Order GLCM

A 3x3x3 Section from an HCC Tumor 3D object

GLCM of the HCC Tumor 3D object

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>0</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>4</th>
<th>7</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>+2</td>
<td>+0</td>
<td>+0</td>
<td>+0</td>
<td>+0</td>
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<tr>
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<tr>
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<td>+4</td>
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<td>+6</td>
<td>+3</td>
<td>+4</td>
<td>+2</td>
<td>+0</td>
</tr>
</tbody>
</table>

Represent different intensity levels:

- Red: +7
- Black: +4
- Blue: +3
- Green: +2
- White: +0

Value to be added to the GLCM cells:

- +value
Features Extraction: Texture Features (cont’d)

A 3*3*3 Section from an HCC Tumor 3D object

2nd Order GLRLM

GLRLM of the HCC Tumor 3D object

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<td>+0</td>
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<td>+0</td>
<td>+1</td>
<td>+0</td>
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<td>+0</td>
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<td>+0</td>
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<tr>
<td></td>
<td>+0</td>
<td>+1</td>
<td>+0</td>
<td>+0</td>
<td>+0</td>
<td>+0</td>
<td>+0</td>
<td></td>
</tr>
</tbody>
</table>

Represent different intensity levels

1 2 3 4 5 6 7 8

Represent different Run Lengths

+value

The value to be added to the GLRLM cells
Examine the functional hyperenhancement (wash-in) and hypo-intensity (wash-out) developed by the HCC regenerative progressive nodules.
In the proposed framework, we used the state-of-the-art spectral analysis employing spherical harmonics (SH) to extract shape features for diagnosing liver tumors.
First, we started assessing the classification performance using individual features. 
Then, we integrated all the extracted features by using concatenation methods obtaining combined features and employed ML classifiers towards the final diagnosis.
## Diagnostic Results

<table>
<thead>
<tr>
<th>Classifier</th>
<th>Approach</th>
<th>Accuracy</th>
<th>AUROC (+ve Class)</th>
<th>Correct Instances</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>B</td>
<td>LR3</td>
</tr>
<tr>
<td><strong>RFs</strong></td>
<td>LOSO</td>
<td>87.1%</td>
<td>0.95</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>10-Fold</td>
<td>85.9%</td>
<td>0.93</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>5-Fold</td>
<td>81.2%</td>
<td>0.88</td>
<td>0.89</td>
</tr>
<tr>
<td><strong>KNN\textsubscript{Fine}</strong></td>
<td>LOSO</td>
<td>85.9%</td>
<td>0.91</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>10-Fold</td>
<td>83.5%</td>
<td>0.91</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>5-Fold</td>
<td>78.8%</td>
<td>0.88</td>
<td>0.74</td>
</tr>
<tr>
<td><strong>SVM\textsubscript{Cub}</strong></td>
<td>LOSO</td>
<td>81.2%</td>
<td>0.89</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>10-Fold</td>
<td>77.6%</td>
<td>0.85</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>5-Fold</td>
<td>77.6%</td>
<td>0.85</td>
<td>0.73</td>
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<tr>
<td><strong>SVM\textsubscript{Quad}</strong></td>
<td>LOSO</td>
<td>84.7%</td>
<td>0.94</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>10-Fold</td>
<td>82.4%</td>
<td>0.93</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>5-Fold</td>
<td>77.6%</td>
<td>0.89</td>
<td>0.80</td>
</tr>
</tbody>
</table>
Diagnostic Results

The confusion matrix shows the following results:

- True Class: Malignant
  - Malignant: 2
  - Intermediate: 11
  - Benign: 4

- True Class: Intermediate
  - Malignant: 2
  - Intermediate: 11
  - Benign: 4

- True Class: Benign
  - Malignant: 0
  - Intermediate: 0
  - Benign: 1

- Predicted Class: Malignant
  - Malignant: 33
  - Intermediate: 0
  - Benign: 1

- Predicted Class: Intermediate
  - Malignant: 2
  - Intermediate: 30
  - Benign: 1

- Predicted Class: Benign
  - Malignant: 2
  - Intermediate: 4
  - Benign: 30
## Diagnostic Results

<table>
<thead>
<tr>
<th>Approach</th>
<th>Accuracy</th>
<th>AUROC</th>
<th>Correct Instances</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>LR1/17 LR2/17</td>
</tr>
<tr>
<td>LOSO</td>
<td>91.2%</td>
<td>0.95</td>
<td>14 17</td>
</tr>
<tr>
<td>10-Fold</td>
<td>88.2%</td>
<td>0.92</td>
<td>13 17</td>
</tr>
<tr>
<td>5-Fold</td>
<td>85.3%</td>
<td>0.90</td>
<td>12 17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>LR4/17 LR5/17</td>
</tr>
<tr>
<td>LOSO</td>
<td>85.3%</td>
<td>0.88</td>
<td>16 13</td>
</tr>
<tr>
<td>10-Fold</td>
<td>82.4%</td>
<td>0.83</td>
<td>15 13</td>
</tr>
<tr>
<td>5-Fold</td>
<td>82.4%</td>
<td>0.83</td>
<td>15 13</td>
</tr>
</tbody>
</table>
• The proposed HCC-CAD system has the ability to provide accurate grading for different hepatic observations according to the LI-RADS guidelines.

• Using the Random Forests classifier with a leave-one-out (LOSO) cross-validation, the developed CAD system achieved an 87.1% accuracy in distinguishing between malignant, intermediate and benign tumors (i.e., First stage classification).

• Using the same classifier and validation, the LR-1 lesions were classified from LR-2 benign lesions with 91.2% accuracy, while 85.3% accuracy was achieved differentiating between LR-4 and LR-5 malignant tumors (i.e., Second stage classification).
Future work

• We have already started to collect a larger subject cohort to optimize the performance of our system in distinguishing and grading multiple hepatic observations at the same classification stage.

• Hepatic observations with LR-M will be added to our dataset to enhance the diagnostic capabilities of our CAD system.

• Automatic segmentation is being developed to reduce the computational time and subjectivity.

• Applying deep learning techniques (e.g., Autoencoder and CNN).
Thank You & Questions