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Applying Quantitative CT Image Feature Analysis to Predict Response of Ovarian Cancer Patients to Chemotherapy

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Abstract

Objective—This study aimed to investigate the role of applying quantitative image features computed from CT images for early prediction of tumor response to chemotherapy in the clinical trials for treating ovarian cancer patients.

Materials and Methods—A dataset involving 91 patients was retrospectively assembled. Each patient had two sets of pre- and post-therapy CT images. A computer-aided detection scheme was applied to segment metastatic tumors previously tracked by radiologists on CT images and computed image features. Two initial feature pools were built using image features computed from pre-therapy CT images only and image feature difference computed from both pre- and post-therapy images. A feature selection method was applied to select optimal features and an equal-weighted fusion method was used to generate a new quantitative imaging marker from each pool to predict 6-month progression free survival. The prediction accuracy between quantitative imaging markers and RECIST criteria was also compared.

Results—The highest areas under ROC curve (AUC) are 0.684 ± 0.056 and 0.771 ± 0.050 when using a single image feature computed from pre-therapy CT images and feature difference computed from pre- and post-therapy CT images, respectively. Using two corresponding fusion-based image markers, AUCs significantly increased to 0.810 ± 0.045 and 0.829 ± 0.043 ($p < 0.05$), respectively. Overall prediction accuracy levels are 71.4%, 80.2%, and 74.7% when using two imaging markers and RECIST, respectively.

Conclusion—This study demonstrated the feasibility of predicting patients' response to chemotherapy using quantitative imaging markers computed from pre-therapy CT images. However, using image feature difference computed between pre- and post-therapy CT images yielded higher prediction accuracy.

Keywords

Quantitative image feature analysis; prediction of tumor response to chemotherapy; chemotherapy of ovarian cancer; Prediction efficacy of clinical trials; Radiomics

1. Introduction

Ovarian cancer has highest mortality rate among all the gynecologic malignancies because majority of the cancers are diagnosed at advanced stage [1]. In order to improve survival rate of ovarian cancer patients after surgeries to remove primary ovarian tumors, applying effective chemotherapy to treat metastasized tumors also plays an important role. As a result, a large number of clinical trials are performed to test new chemotherapy drugs and/or procedures. However, since the metastasized tumors are typically P53 driven and genetically instable [2], responses to the chemotherapy vary significantly across the individual patients. In order to improve efficacy of clinical trials, it remains a big challenge of how to effectively identify patients who are likely to receive benefit from the clinical trials at early stage.

To address this clinical challenge, extensive research efforts have been conducted to develop and test variety of imaging modalities for monitoring or predicting tumor response to chemotherapies [3–6]. For example, one review article [7] compared many modalities for imaging ovarian cancer and peritoneal metastases including CT, PET/CT, diffusion-weighted MRI, dynamic contrast-enhanced MRI, and magnetic resonance spectroscopy (MRS), ultrasound (US) and optical imaging. It reviewed a large number of studies performed from 1980 to 2010 for ovarian cancer diagnosis, evaluation of response to therapies, surveillance and detection of cancer recurrence. The study summarized that CT had superior advantages including wide availability, good reproducibility, high cost-efficiency, and fast image scanning time. Only US is lower in cost than CT, but its accuracy is much lower than CT [8]. Although MRI may provide additional functional information, it has equivalent performance in detecting and staging abdominal-pelvic disease to CT, but the high-cost and longer examination times precludes the use of MRI for most ovarian cancer patients [9]. Thus, CT is the only imaging modality routinely used in current clinical practice for ovarian cancer diagnosis and treatment evaluation [8].

Accordingly, during the course of clinical trial, sequential CT images are acquired pre-therapy and post-therapy including the first post-therapy CT scan acquired 6 weeks after starting the therapy to monitor tumor response to the therapy based upon the Response Evaluation Criteria in Solid Tumors (RECIST 1.1) guidelines, which allows to evaluate tumor size variation of up to 5 metastatic tumors (or 2 per organ) depicting on pre- and post-therapy CT images [10]. However, a significant limitation of RECIST criteria is that it does not accurately evaluate the changes in tumor volume, density and its heterogeneity. As a result, previous studies have reported that RECIST assessments often did not correlate well with clinical outcomes [11, 12].

To address the clinical limitations of lacking effective clinical markers when using CT images, we investigated the feasibility of identifying new quantitative imaging markers computed from CT images to predict patient response to the chemotherapy at an early stage. The overall objectives of this new study are to investigate 1) the potential utility of applying a new quantitative imaging feature analysis method and clinical marker acquired from pre-therapy CT images and/or adding early post-therapy CT images to predict response of ovarian cancer patients to chemotherapy; and 2) compare the prediction performance

between using new quantitative imaging markers and the RECIST criteria for assessing patients' response to the chemotherapy.

2. Materials and methods

Using an institutional review board (IRB) approved study protocol, we retrospectively assembled a dataset involving 91 ovarian cancer patients who were recruited to participate in clinical trials to test new chemotherapy drugs or procedures at our University Medical Center. 30 out of the 91 patients was reported in prior study [13] which initially investigated the quantitative image features for chemotherapy response assessment. The current study expands previous dataset by adding 61 patients. The data inclusion criteria are as follows: 1) diagnosis of recurrent, high grade (serous, endometrioid, undifferentiated) ovarian/peritoneal/tubal carcinoma; 2) receiving systemic chemotherapy; 3) having pre- and post-therapy CT imaging scans in which the first post-therapy CT scan was performed 4 to 6 weeks after initiation of therapy.

All CT images were acquired using standard CT scanning image acquisition protocol on a GE Light Speed VCT 64-row detector or GE Discovery 600 16-row detector machine. The protocol of the CT scans included the following parameters: 1) X-ray power output is set at 120 kVp with a variable current range from 100 to 600mA depending on patient body size. 2) The 100cc contrast agent of iopamidol (Iovue 370, Bracco Diagnostics, Inc.) is injected at a rate of 2-3 cc/sec through a 20-gauge IV needle placed at the antecubital fossa. 3) Helical axial images of the chest, abdomen and pelvis are performed at 60 sec after contrast agent injection. 4) Images are acquired at pitch of 1.375, slice thickness of 5 mm, and reconstructed to 1.25 mm to make sagittal and coronal reformats at 2.5 mm; sagittal and coronal reconstructed images are also performed at 2.5 mm. Clinical data including radiologists' rated response based on RECIST criteria and 6-month progression free survival (PFS), which is a standard evaluation index approved by US Food and Drug Administration and European Medicines Agency for evaluating efficacy of testing new cancer chemotherapies in the clinical trials [14], were also collected to allow for performance comparison. Patient characteristics are summarized in Table 1. Although all patients were survived in the 6-month course of clinical trials, 52 patients maintained 6-month PFS, while 39 exhibited no response to the therapies with progressive diseases after completion of the clinical trials.

In order to compute quantitative image features, we applied a previously developed computer-aided detection (CAD) scheme [15] to segment the tumors, which were previously tracked and assessed by radiologists using the RECIST criteria. The segmentation results were visually assessed and manually corrected using a Graphic User Interface (GUI) tool when necessary. Figure 1 illustrates four tumor regions with CAD-marked boundary contour depicting on CT image slices.

From the volumetric data of each segmented tumor in multiple CT image slices, CAD scheme initially computed 159 features, which can be divided into four groups as shown in Table 2. The first group includes 10 tumor shape based features described in Ref [16, 17]. These features estimate the tumor volume and volume based shape distortions. Nine out of

the ten features are computed based on the segmented 3D tumors, and only one (Convexity) is a 2D feature, which is computed from the central slice. The second group computes 21 tumor density based features, which are commonly used statistical features [18] to quantify the CT number distribution and heterogeneity inside the tumor volume. The third group measures tumor texture based features. Among them, 11 different 2D gray scale run length features are computed in 4 different directions (0° , 45° , 90° , and 135°) [19, 20] of the central slice. The fourth group computes features based on wavelet transform on each CT slice, which allows for decomposing the image into 4 components, I_{LL} , I_{LH} , I_{HL} , and I_{HH} , where H and L are labeled as the high or low scale decomposition in either X or Y direction (Figure 2). We utilized the “Coiflet 1” Wavelet previously described in the literature for wavelet transformation [18]. As such, in this computation, I_{LH} denotes the component after applying the low scale and high scale filter along the X and Y direction, respectively. For each component, we then recalculated the density features computed in Group 2.

For each case, CAD scheme computed the same 159 image features from two sets of CT images acquired from pre-therapy (F_i^{Pre}) and the first post-therapy (F_i^{Post}). In addition, tumor feature difference ΔF_i between two sets of pre- and post-therapy CT images was also computed [$\Delta F_i = F_i^{\text{Post}} - F_i^{\text{Pre}}$]. All image features or feature differences were normalized into the range of 0 to 1 based on a linear scaling between $\mu + 2\sigma$ and $\mu - 2\sigma$, where μ and σ denote the mean and standard deviation of the feature values computed from all tracked and segmented lesions in our dataset, respectively. Since in accordance with RECIST criteria, 1 to 5 tumors were identified and serially measured by radiologists, the average feature computed from M tumors ($1 \leq M \leq 5$) was also computed and used to represent the final case-based feature value. We used these case-based features to predict the 6-month PFS of the patients.

We built two initial feature pools namely, the first one includes image features computed from pre-therapy CT images only (F_i^{Pre}) and the second one includes image feature difference computed between two sets of post- and pre-therapy CT images (ΔF_i). Then, we evaluated the performance of each feature by computing the area under the Receiver Operating Characteristic (ROC) curve method (AUC) [21]. First, we sorted all features based on computed AUC values and selected 12 best performers from each feature pool. We also compared whether using feature difference ΔF_i could yield a significantly higher performance than using the features computed from pre-therapy CT images only. Next, we applied a nearest neighbor error algorithm [22] to independently select the optimal image feature candidates from two initial feature pools (F_i^{Pre} and ΔF_i). The selected feature candidates were evaluated and adjusted to create an optimal feature cluster. Two equal-weighted fusion models were built to combine the final optimal features selected from F_i^{Pre} and ΔF_i feature pools. The prediction score generated by each fusion model is used as a new quantitative imaging prediction marker. Finally, we applied two evaluation indices to assess performance of two new quantitative imaging markers generated using optimal features independently selected from F_i^{Pre} and ΔF_i feature pools to predict 6-month PFS of ovarian

cancer patients. The first evaluation index is AUC of ROC curve and the second index is an overall prediction accuracy computed from a confusion matrix, which is generated by applying a threshold to the quantitative imaging marker scores. In addition to two confusion matrices generated using F_1^{Pre} and ΔF_1 features, we also generated the third confusion matrix using prerecorded radiologists' assessment results based on RECIST criteria in which PD (progression disease) was assigned as non-responsive (No to 6-month PFS), while other three RECIST ratings were assigned as responsive group (Yes to 6-month PFS). The overall prediction accuracy levels of using 2 imaging markers and radiologists' assessment were then compared.

3. Results

Table 3 summarizes two sets of 12 best performed image features computed from pre-therapy CT images only and difference of two CT image sets acquired pre- and post-therapy. The first set of using pre-therapy CT images only consists of 4 tumor density features (Skewness, Uniformity, Entropy, and Kurtosis), 6 wavelet features (Contrast-LH, Contrast-HL, Skewness-HH, Density standard deviation, ratio-HL, Kurtosis-HL, Mean contrast-LH), and 2 tumor shape features (Sphericity and Compactness 2). AUC values of these 12 features range from 0.592 to 0.684. The best performed feature within this group is Skewness with an AUC value of 0.684 ± 0.056 . The second set includes 7 tumor density features (Energy, Median, Rms, Average density, Maximum density, and Density range), 3 wavelet features (Fluctuation std-LL, Entropy-LL, and Energy-HH), and 3 tumor shape features (Compactness 1, Tumor volume, and Surface area). AUC values of using these 12 features ranged from 0.670 to 0.770, among which the feature of Compactness yielded the highest AUC value of 0.770 ± 0.050 .

After applying the nearest neighbor error algorithm, 4 and 8 image features were ultimately selected from the two described feature sets of using (1) pre-therapy CT images only and (2) both pre- and post-therapy images, respectively, to build two fusion-based quantitative imaging markers. As indicated in Figure 3, two imaging markers yielded AUC value of 0.810 ± 0.045 and 0.829 ± 0.043 , respectively. Both AUC values are significantly higher than using the best single image feature in the two initial feature pools ($p < 0.05$). However, two AUCs computed from two fusion-based imaging markers are not statistically significant ($p = 0.127$).

Table 4 shows and compares three confusion matrices generated using two quantitative imaging markers and prerecorded radiologists' assessment using RECIST criteria, respectively. The overall prediction accuracy levels are 71.4% (65/91), 80.2% (73/91), and 74.7% (68/91) when using two imaging markers and radiologists' assessment, respectively. The result showed that using quantitative imaging marker computed from both pre- and post-therapy CT images yielded the highest accuracy. The results also showed that radiologists' assessment tended to rate highest number of cases into responsive (6-month PFS) group. As a result, radiologists' assessment has lower positive predictive value (PPV) and highest negative predictive value (NPV). Three PPV values are 0.78 (36/46), 0.78

(47/60) and 0.69 (52/75), while three NPV values are 0.64 (29/45), 0.84 (26/31) and 1.00 (16/16) when using two imaging markers and radiologists' assessment, respectively.

4. Discussion

Identifying new quantitative imaging markers to improve accuracy of predicting cancer prognosis and treatment efficacy has been attracting extensive research interest recently in order to assist developing precision medicine [23]. In this study, we investigated the feasibility of applying a new quantitative image feature analysis method to predict the response to chemotherapies at an early stage for treating ovarian cancer patients participated in the clinical trials. Although a number of previous studies have been conducted to develop new quantitative imaging markers to predict clinical trial efficacy of treating ovarian cancer patients [13, 24–26], this study has two unique characteristics. First, we identified a new quantitative imaging marker to predict clinical outcome (6-month PFS) using pre-therapy CT images only. Second, by adding an early post-therapy CT scan, we identified the second imaging marker based on the image feature difference between two sets of CT scans.

From the study results, we made following observations. First, pre-therapy CT imaging data also includes useful information for prediction of response to chemotherapies. Similar to the results yielded from assessing treatment efficacy of breast and lung cancers [27, 28], the results of this study also support an emerging concept of Radiomics which hypothesizes that the quantified tumor heterogeneity related image features enabled to predict a clinical phenotype that associates well to the genomic and/or biologic biomarkers in predicting cancer prognosis and response to the treatment [18]. In this study, we found that a number of tumor density and heterogeneity-related image features, computed from the pre-therapy CT images only, had a significantly higher discriminatory power than random guess ($AUC = 0.5$). As shown in the left column of Table 3, the highest AUC value of 0.684 ± 0.056 was achieved by tumor density Skewness. Furthermore, by fusing a cluster of 4 selected optimal image features using an equal-weighting method, the predictive performance significantly increased to 0.810 ± 0.045 ($p < 0.05$). Thus, if successful, this new imaging marker can provide clinicians (e.g., oncologists) a new quantitative tool to identify or select patients who will benefit from the chemotherapy in the clinical trials and avoid unnecessary toxicity to the patients who will not respond to the chemotherapies before starting clinical trials.

Second, we observed that similar to RECIST guidelines used in current clinical practice, which require comparison of tumor size variation between pre- and post-therapy, adding quantitative image features computed from post-therapy CT images can provide more discriminatory information. The new quantitative imaging marker generated from feature difference between pre- and post-therapy yielded higher prediction performance than using either imaging marker computed from pre-therapy images only or RECIST-guided assessment method (80.2% vs. 74.7%). The higher performance indicates that adding image features related to tumor shape (compactness) and density heterogeneity changes is helpful to more accurately predict tumor response to chemotherapy than using tumor size variation alone in RECIST guidelines.

Third, using quantitative imaging markers not only has the potential to yield higher prediction accuracy, it also provides complementary or supplementary information to radiologists' assessment based on RECIST guidelines. As shown in Table 4, using quantitative imaging markers yielded higher PPV, while using RECIST yielded higher NPV. As a result, due to the lower correlation between the new quantitative imaging marker and existing RECIST approaches, this may provide a new opportunity for both research and clinical communities to develop and test a new method to optimally combine information from both assessment or prediction methods to achieve further improved prediction accuracy in future clinical practice.

While our results are encouraging, this study has a number of limitations. First, due to the small dataset with 91 cases, we only tested a simple equal-weighted fusion method to generate imaging markers, which is not optimal approach. As the increase of dataset size in future study, an optimal machine learning method should be applied to optimally combine image features and generate new imaging markers. Second, although the addition of the post-therapy CT image data can significantly improve the predicting performance of single feature, the performance improvement between two fusion based image markers was not statistically significant. The reason behind this observation needs to be further investigated using other independent image datasets. Third, for each case, our computer-aided detection scheme only segments and analyzes the tumors previously marked and tracked by the radiologist based on RECIST guideline. Although the metastasized tumors can locate in different organs or abdominal-pelvic regions and their image features may be different, the tumor shape and/or density heterogeneity is unique characteristic to predict response of the metastasized tumors to chemotherapy [18]. To minimize such impact, we computed the average feature value as the final case-based feature. We recognized that this simple averaging method might not be the optimal method. Thus, we still need to investigate the more effective algorithms to identify more clinically relevant tumors [25] and optimally generate the case-based image features. Fourth, in this dataset, the patient cases were not classified with different chemotherapy drugs or different histopathology types. Given that some characteristics may be specific for assessing the response of a certain tumor pathology/chemotherapy drug type combination, dividing and finding the best features for the patients with different therapy/pathology groups may further improve the predicting accuracy. Last, although the robustness of applying the quantitative image marker generated from pre- and post-therapy CT images was initially demonstrated as comparing to our previous study using only 30 cases [13], the size of current dataset of 91 cases remains small. Thus, the robustness of our experiment results need to be further tested and verified using large and diverse image datasets in the future.

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References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *Ca-a Cancer Journal for Clinicians*. 2016; 66:7–30. [PubMed: 26742998]
2. The Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. *Nature*. 2011; 474:609–615. [PubMed: 21720365]
3. Tempany CMC, et al. Staging of advanced ovarian cancer: Comparison of imaging modalities - report from the radiological diagnostic oncology group. *Radiology*. 2000; 215:761–767.
4. Gu P, Pan LL, Wu SQ, et al. CA 125, PET alone, PET-CT, CT and MRI in diagnosing recurrent ovarian carcinoma: a systematic review and meta-analysis. *European Journal of Radiology*. 2009; 71:164–174. [PubMed: 18378417]
5. Kyriazi S, Kaye SB, deSouza NM. Imaging ovarian cancer and peritoneal metastases-current and emerging techniques. *Nature Reviews Clinical Oncology*. 2010; 7:381–393.
6. Fischerova D, Burgetova A. Imaging techniques for the evaluation of ovarian cancer. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2014; 28:697–720. [PubMed: 24846098]
7. Kyriazi S, Kaye SB, deSouza NM. Imaging ovarian cancer and peritoneal metastases-current and emerging techniques. *Nature Reviews Clinical Oncology*. 2010; 7:381–393.
8. Fischerova D, Burgetova A. Imaging techniques for the evaluation of ovarian cancer. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2014; 28:697–720. [PubMed: 24846098]
9. Foti PV, Attina G, et al. MR imaging of ovarian masses: classification and differential diagnosis. *Insights into Imaging*. 2016; 7:21–41. [PubMed: 26671276]
10. Eisenhauer EA, et al. New response evaluation criteria in solid tumours: Revised recist guideline (version 1.1). *European Journal of Cancer*. 2009; 45:228–247. [PubMed: 19097774]
11. Sharma MR, Maitland ML, Ratain MJ. Recist: No longer the sharpest tool in the oncology clinical trials toolbox point. *Cancer Res*. 2012; 72:5145–5149. [PubMed: 22952219]
12. Abramson RG, McGhee CR, Lakomkin N, Arteaga CL. Pitfalls in recist data extraction for clinical trials: Beyond the basics. *Academic Radiology*. 2015; 22:779–786. [PubMed: 25794800]
13. Qiu YC, Tan M, McMeekin S, Thai T, Ding K, Moore K, Liu H, Zheng B. Early prediction of clinical benefit of treating ovarian cancer using quantitative ct image feature analysis. *Acta Radiologica*. 2016; 57:1149–1155. [PubMed: 26663390]
14. Fallowfield LJ, Fleissig A. The value of progression-free survival to patients with advanced-stage cancer. *Nature Reviews Clinical Oncology*. 2012; 9:41–47.
15. Danala G, Wang Y, Thai T, et al. Improving efficacy of metastatic tumor segmentation to facilitate early prediction of ovarian cancer patients' response to chemotherapy. *Proc SPIE*. 2017; 10065:100650J-1-6.
16. te Brake GM, Karssemeijer N, Hendriks J. An automatic method to discriminate malignant masses from normal tissue in digital mammograms. *Physics in Medicine and Biology*. 2000; 45:2843–2857. [PubMed: 11049175]
17. Zheng B, et al. A method to improve visual similarity of breast masses for an interactive computer-aided diagnosis environment. *Medical Physics*. 2006; 33:111–117. [PubMed: 16485416]
18. Aerts H, et al. Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach. *Nature Communications*. 2014; 5:4006.
19. Haralick RM, Shanmugam K, Dinstein I. Textural features for image classification. *Ieee Transactions on Systems Man and Cybernetics*. 1973; SMC3:610–621.
20. Tang XO. Texture information in run-length matrices. *Ieee Transactions on Image Processing*. 1998; 7:1602–1609. [PubMed: 18276225]
21. Metz CE, Herman BA, Shen JH. Maximum likelihood estimation of receiver operating characteristic (roc) curves from continuously-distributed data. *Statistics in Medicine*. 1998; 17:1033–1053. [PubMed: 9612889]
22. Heijden FvdD, Robert, Ridder, Dick, Taxa, David. Classification, parameter estimation and state estimation: An engineering approach using matlab. John Wiley & Sons; 2004.
23. Collins FS, Varmus H. A new initiative on precision medicine. *The New England Journal of Medicine*. 2015; 372:793–795. [PubMed: 25635347]

24. Wang Y, Thai T, Moore K, Ding K, McMeekin S, Liu H, Zheng B. Quantitative measurement of adiposity using CT images to predict the benefit of bevacizumab-based chemotherapy in epithelial ovarian cancer patients. *Oncology Letter*. 2016; 12:680–686.
25. Tan M, Li Z, Qiu Y, McMeekin S, Thai T, Ding K, Moore K, Liu H, Zheng B. A new approach to evaluate drug treatment response of ovarian cancer patients based on deformable image registration. *IEEE Transactions on Medical Imaging*. 2016; 35:316–325. [PubMed: 26336119]
26. Wang Y, Qiu Y, Thai T, Moore K, Liu H, Zheng B. A two-step convolutional neural network based computer-aided detection scheme for automatically segmenting adipose tissue depicting on CT images. *Computer Methods and Programs in Biomedicine*. 2017; 144:97–104. [PubMed: 28495009]
27. Aghaei F, Tan M, Hollingsworth AB, Zheng B. Applying a new quantitative global breast MRI feature analysis scheme to assess tumor response to chemotherapy. *Journal of Magnetic Resonance Imaging*. 2016; 44:1099–1106. [PubMed: 27080203]
28. Yan S, Qian W, Guan Y, Zheng B. Improving lung cancer prognosis assessment by incorporating synthetic minority oversampling technique and score fusion method. *Medical Physics*. 2016; 43(6):2694–2703. [PubMed: 27277016]

Figure. 1.
Four examples of the tumor segmentation with marked boundary contours.

Figure. 2.

The scheme of the applying the un-decimated wavelet transform on the target CT slices

Figure. 3. Comparison of two sets of ROC curves generated by fusion-based quantitative imaging markers (Ave) and the best single feature computed from the pre-therapy CT images only (a) and from both pre-and post-therapy CT images (b).

Table 1

Patient information for both PFS “Yes” and “No” groups

6-month PFS	Yes	No
Number of patients	52	39
Patient average age	66 ± 8	67 ± 9
Number of totally tracked metastatic tumors	101	96
Average tumor diameter (before therapy)	27 mm	24 mm

Table 2

List of the computed 159 image features in 4 groups for estimating tumor characteristics

Feature class	Feature number	Feature description
Shape	1-10	Volume, convexity, maximum radius, radius standard deviation(STD), surface area, compactness feature 1, compactness feature 2, maximum 3D diameter, spherical disproportion, spherical ratio, ratio of surface area to volume
Density	11-31	Density, density STD, gradient mean, gradient STD, iso-intensity, fluctuation mean, fluctuation STD, mean contrast, contrast, skewness, kurtosis, STD ratio of tumor to boundary, energy, entropy, maximum intensity, mean absolute deviation, median, minimum, range, rms, uniformity
Texture	32-75	11 gray level run length based features in on four directions (0°, 45°, 90°, and 135°) (Defined in ref [20, 21])
Wavelet	76-159	Apply the density features on the four wavelet decompositions [19].

Table 3

The summary of the areas under ROC curve (AUCs) of using each of 12 best performed image features computed from using pre-therapy CT images only and image feature difference computed between pre- and post-therapy CT images to predict 6-month PFS.

Pre-treatment feature group	Performance	Pre-post treatment feature group	Performance
Skewness	0.684±0.056	Compactness 1	0.771±0.050
Contrast-LH	0.652±0.059	Volume	0.755±0.051
Contrast-HL	0.643±0.058	Surface area	0.739±0.052
Uniformity	0.637±0.058	Fluctuation std-LL	0.711±0.054
Skewness-HH	0.623±0.059	Energy	0.707±0.055
Sphericity	0.621±0.058	Median	0.695±0.054
Entropy	0.619±0.059	Entropy-HL	0.687±0.055
Density std ratio-HL	0.618±0.058	Rms	0.685±0.055
Kurtosis-HL	0.615±0.059	Density	0.684±0.055
Compactness 2	0.602±0.059	Maximum density	0.682±0.056
Mean contrast-LH	0.596±0.060	Density range	0.677±0.056
Kurtosis	0.592±0.060	Energy-HH	0.670±0.057

Summary of three confusion matrices to predict 6-month PFS using two fusion-based quantitative imaging (QI) markers and pre-recorded radiologists' assessment results based on RECIST criteria.

Table 4

		QI Marker based on Pre-therapy CT Images Only		QI Markers based on Both Pre- and Post-therapy CT Images		Radiologists' Assessment Using RECIST Criteria	
<u>6-month PFS</u>		Yes	No	Yes	No	Yes	No
Prediction							
Yes		36	10	47	13	52	23
No		16	29	5	26	0	16