Does GRASP affect DCE-MRI for assessing response to neoadjuvant chemotherapy in patients with esophageal cancer?

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Abstract

Purpose To compare the value of two dynamic contrast-enhanced Magnetic Resonance Images (DCE-MRI) reconstruction approaches, namely golden-angle radial sparse parallel (GRASP) and view-sharing with golden-angle radial profile (VS-GR) reconstruction, and explore their values in assessing response to neoadjuvant chemotherapy (nCT) in esophageal cancer (EC).

Methods The study prospectively enrolled EC patients receiving nCT before surgery. DCE-MRI scanning was performed after nCT and within 1 week before surgery. Chemotherapy response was assessed according to Tumor Regression Grade (TRG), and patients were stratified into a responsive group (TRG1+2) and a non-responsive group (TRG3+4+5). Wilcoxon test was utilized for comparing GRASP and VS-GR reconstruction, and Kruskal-Wallis and Mann-Whitney test was performed for each parameter to assess response, and Spearman test was performed for analyzing correlation between parameters and TRGs, as well as responder and non-responder. Results Among the 64 patients included in this cohort (52 male, 12 female; average age of 59.1±7.9 years), 4 patients showed TRG1, 4 patients were TRG2, 7 patients were TRG3, 11 patients were TRG4, and 38 patients were TRG5. They were stratified into 8 responders and 56 non-responders. A total of 15 parameters were calculated from each tumor. With VSGR, 10/15 parameters significantly correlated with TRG and response groups. Of these, only AUCmax showed moderate correlation with TRG, 7 showed low correlation and 2 showed negligible correlation with TRG. 8 showed low correlation and 2 showed negligible correlation with response groups. With GRASP, 13/15 parameters significantly correlated with TRG and response groups. Of these, 10 showed low correlation and 3 showed negligible correlation with TRG. 11 showed low correlation and 2 showed negligible correlation with TRG.

Conclusion In patients with esophageal cancer on neoadjuvant chemotherapy, several
parameters can differentiate responders from non-responders, using both GRASP and VS-GR techniques. GRASP may be able to better differentiate these two groups compared to VS-GR.

Introduction

The incidence rate of esophageal cancer (EC) is rising rapidly worldwide, and it has become the eighth most common cancer (1). It is difficult to suspect early EC until progressive dysphagia develops. As symptoms develop, the disease is often in the intermediate and advanced stages. Patients with resectable EC continue to have poor outcome, with 5-year overall survival ranging from 15% to 34% (2). Preoperative neoadjuvant chemotherapy (nCT) had been shown to have both overall and disease-free survival benefit over surgery alone in patients with EC (2, 3).

In China, squamous cell carcinoma (SCC) is the main pathological type of EC, and is a high-grade malignancy with rapid progression, poor response to treatment and high recurrence rate (4, 5). Moreover, the disease is associated with poor prognosis, limited quality of life after surgery (6) and a high incidence of postoperative morbidity and mortality (7-9). Ando et al. reported that nCT before resection is currently the main treatment for stages II and III SCC (9, 10). The authors also suggested that if local tumor control is achieved, nCT followed by surgical procedures is an optimum treatment strategy, which can improve overall survival for patients with SCC (10). Predicting response to nCT accurately helps clinicians to provide the best treatment such as modification of nCT, or termination of nCT to initiate a resection (1, 3).

18 F-fluorodeoxyglucose positron emission tomography (18 F-FDG-PET) seems to be a promising technique for predicting therapeutic response, but more work is required in standardizing protocols and the time of scanning (11). Dynamic contrast-enhanced Magnetic Resonance Images (DCE-MRI) had also showed been shown to have the ability to
predict an early response in EC following 3 weeks of concurrent chemoradiotherapy in limited cases (12, 13). It is still challenging to non-invasively predict response to nCT. Recently, golden-angle radial sparse parallel (GRASP) MRI has gained interest, and has been applied to imaging of liver, rectal cancer and renal cell carcinoma (14-17). GRASP is capable of reconstructing the acquired data at very high temporal resolution using only a small number of radial spokes for every temporal frame. This enables high-resolution free-breathing perfusion imaging with higher in-plane spatial resolution and thinner partitions resulting in near-isotropic resolution, compared with the current view-sharing with golden-angle radial profile (VS-GR) reconstruction, without the current imaging constraints of breath-holding techniques (14).

The objective of this study was to compare DCE-MRI with GRASP reconstruction against DCE-MRI with VS-GR reconstruction in assessing response to nCT in patients with EC and to identify DCE-MRI parameters which can differentiate responders from non-responders

Methods And Materials

The prospective study was approved by the Ethics Committee, and written informed consent was obtained from all participants. This cohort enrolled patients who received nCT followed by surgical resection. DCE-MRI was obtained within 1 week before surgery. All studies were performed between September 2015 and March 2017. The inclusion criteria were: i) Patients were pathologically confirmed with stage II-III (18, 19) EC by esophagoscopy, ii) patients received clinical and imaging response evaluation at 2 weeks after completing all the treatment courses. iii) All patients received 2 cycles (21 days each) of nCT (Paclitaxel and Nedaplatin) before surgery (Fig 1).

DCE-MRI Scanning methods

MRI examination was performed on a 3 T MR scanner (MAGNETOM Skyra, Siemens Healthcare) with free breathing dynamic contrast-enhanced Radial VIBE using an 18-
element body matrix coil and an inbuilt 32-element spine matrix coil. Radial VIBE sequence parameters were following: TR=3.98ms, TE=1.91ms, flip angle=12°, acquisition matrix=300×300, FOV=300mm×300mm×146mm, slice thickness=3mm, reconstructed image voxel size=1.0×1.0×3.0 mm3, radial views=1659, scanning time=309s. A total of 68 period s and 4896 images were collected, and each period included 72 images, which covered the whole chest during free breathing. Time resolution of the first 61 periods was 2.4s, and that of the last 7 periods was 21.7s. At 20 seconds after the beginning of scanning, 10-15mL Gadopentetate Dimeglumine Injection (0.2 ml/kg of body weight, Omniscan, GE Healthcare) was injected at a rate of 2.5mL/s by a MR-compatible automated double-tube high-pressure injector (Spectris Solaris EP, Medrad), followed by equal volume of normal saline solution to flush the tube.

Histopathology response

Pathologic response was stratified into 5 grades according to Tumor Regression Grade (TRG) (20): TRG 1 (complete regression) showed absence of residual cancer and fibrosis extending through the different layers of the esophageal wall; TRG 2 was characterized by the presence of rare residual cancer cells scattered through the fibrosis; TRG 3 was characterized by an increase in the number of residual cancer cells, but fibrosis still predominated; TRG 4 showed residual cancer outgrowing fibrosis; and TRG 5 was characterized by absence of regressive changes. They were stratified into a responsive group (TRG1+2) and a non-responsive group (TRG3+4+5).

Image Processing and Data Analysis

From DCE-MRI, 1659 of stack-of-stars views were acquired. These radial views were input into online reconstruction pipeline of view sharing reconstruction and regrouped into 2 sub-frames (sub-frame-1: T0-T61 with a temporal resolution of 2.4s, sub-frame 2 from T62-T68 with temporal resolution of 21.7s). GRASPs were performed offline using a home setup
of GRASP reconstruction processing pipeline (https://mrirecon.github.io/bart/) running on a Yarra server (https://yarra.rocks), with the same data but using a temporal resolution of 4.5s. Details on both reconstructions were summarized in Table 1.

The images reconstructed by two different approaches, namely GRASP and VS-GR, were processed by Omni-Kinetics software (GE Medical, China) to segment the tumor and generate pharmacokinetic parameters respectively. Since the esophageal artery is not easy to identify, the thoracic aorta was selected to obtain the arterial input function (AIF). Figure 2 shows the AIFs derived from GRASP and VS-GR reconstructions from the same contrast-enhanced study.

The 3D- regions of interest (ROI) was segmented manually by two radiologists with more than 10 years experiences in thorax radiology. The radiologists were blinded to clinical data, and were asked to include the entire tumor on each slice post-nCT, except areas of cystic or necrotic degeneration and normal blood vessels. Tofts model was used to generate the pharmacokinetic parameters.

Statistical Analysis

SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA) were used to perform statistical analysis in this study. Interobserver reproducibility of radiomic feature extraction was assessed by inter-class correlation coefficients (ICCs). An ICC > 0.75 was considered good agreement. The Wilcoxon test of was used to compare the various parameters between VS-GR and GRASP reconstruction, and Kruskal-Wallis test for DCE-MRI parameters with VS-GR or GRASP reconstruction among the TRG1-5 groups (P<0.05). Mann-Whitney test was for analyzing the differences between responder and non-responder groups. Spearman test was performed for correlation analysis between DCE-MRI parameters and TRGs, or response groups. Spearman’s correlation coefficients were assessed as follows: a correlation coefficient of 0.90–1.00 is considered very high; 0.70–0.89, high; 0.50–0.69,
Among the total of 64 patients (52 male, 12 female; average age of 59.1±7.9 years), 59 patients had SCC, 2 patients had adenocarcinoma and 3 patients had adenosquamous carcinoma. According to pathologic response, 4 patients showed TRG1, 4 patients were TRG2, 7 patients were TRG3, 11 patients were TRG4, and 38 patients were TRG5. They were stratified into 8 responders and 56 non-responders (Table 2).

ICCs showed the excellence of 15 pharmacokinetic parameters from the two reconstructions as assessed by the two radiologists, and the kappa value was 0.918.

Comparison of DCE-MRI parameters with VS-GR and GRASP reconstruction groups

GRASP showed a better AIF curve with steeper slope and sharp peak compared to VS-GR (Figure 2). A total of 15 pharmacokinetic parameters were extracted from each tumor. 14 of these showed statistically significant difference for both VS-GR and GRASP reconstruction across the TRG groups. Only plasma volume fraction (Vp) max did not show a significant difference (P=0.628).

Comparison among TRG1-5 for DCE-MRI parameters with VS-GR and GRASP reconstruction

14/15 DCE-MRI parameters both with VS-GR and with GRASP reconstruction showed significance inter-groups by TRG 1-5 (P<0.05), except for Ve max showed not significant inter-groups by TRG 1-5 (Table 3).

Comparison between responder and non-responder groups for DCE-MRI parameters with VS-GR/GRASP reconstruction

Ten parameters with VS-GR reconstruction showed significant differences between responders and non-responders, which including volume transfer constant (Ktrans) max, Ktrans mean, Ktrans 75%, intravasation rate contrast (Kep) max, extravascular extracellular volume fraction (Ve) mean, Ve 75%, Vp max, the initial area-under-the-
concentration versus time curve (AUC) max, AUC mean, AUC 75%. 13 parameters with GRASP reconstruction showed significant differences between responders and non-responders, which including Ktrans max, Ktrans mean, Ktrans 75%, Kep max, Kep mean, Ve mean, Ve 75%, Vp max, Vp mean, Vp 75%, AUC max, AUC mean, AUC 75% (Table 4). Correlation between parameters with VS-GR/GRASP reconstruction and TRG/response. With VSGR, 10/15 parameters significantly correlated with TRG and response groups. Of these, only AUCmax showed moderate correlation with TRG, 7 showed low correlation and 2 showed negligible correlation with TRG. 8 showed low correlation and 2 showed negligible correlation with response groups. With GRASP, 13/15 parameters significantly correlated with TRG and response groups. Of these, 10 showed low correlation and 3 showed negligible correlation with TRG. 11 showed low correlation and 2 showed negligible correlation with TRGs (Table 5).

Discussion

This study demonstrated that GRASP reconstruction may affect the results of DCE-MRI, DCE-MRI with VS-GR and GRASP reconstruction could assess tumor response, and pharmacokinetic parameters with GRASP and VS-GR reconstruction may help stratify responders from non-responders in patients with EC treated by nCT. In this study, 10 post-nCT pharmacokinetic parameters with VS-GR reconstruction and 13 parameters with GRASP reconstruction showed statistically significant differences between responders and non-responders. Most DCE-MRI studies only analyzed parts of parameters, such as Ktrans mean, kep mean, Ve mean, and AUC, and showed DCE-MRI could assess the response to therapy (22). In the current study, we tried to analyze more parameters acquired from DCE-MRI, and 15 parameters were analyzed. DCE-MRI with GRASP reconstruction could provide higher in-plane spatial resolution and
near-isotropic resolution (14). Contribution to the VS-GR images with a 2.1s apparent temporal resolution is from a ~21s time footprint acquisition, while GRASP is reconstructed from a 4.5s time footprint, higher temporal resolution normally leads to an improved AIF, which is used for close-to-true pharmacokinetics parameters calculation (23). This could potentially result in better acquisition of pharmacokinetic parameters compared to conventional VS-GR DCE-MRI, which has been reported in hepatocellular carcinoma (14), renal cell carcinoma (17), and rectal cancer (16). VS-GR DCE-MRI had been used in EC (13). However, GRASP reconstruction has not been compared with it. The AIF for the pharmacokinetic models plays an important role in determining the quantitative measurements of physiological parameters, where small differences in AIF may lead to large differences in quantitative maps and higher temporal resolution gives smaller differences.

More parameters with GRASP showed significant correlation with TRGs and response groups than those with VS-GR reconstruction. Both 10/15 parameters with VS-GR reconstruction showed significant correlation with TRGs and response groups, and both 13/15 parameters with GRASP reconstruction showed significant correlation with TRGs and response groups. It may be the effect of GRASP reconstruction, providing higher time resolution and more information.

AUCmax showed the only moderate correlation with TRG in the results,

Detecting residual cancer post-nT is critical. Fortunately, some pharmacokinetic parameters between TGRs showed significant differences in this study. The information of whole tumor, rather than a single axial level, was assessed in our study, which theoretically provides a more representative picture of tumor information than that provided by single-level analysis.

FDG-PET have been used for neoadjuvant treatment response assessment in EC(24), and
the FDG-PET response after neoadjuvant treatment could predict the pathological response and seems to be related to survival (25-27). However, Van Rossum et al. showed that accuracy of imaging is insufficient in predicting pathologic response (28), and the prognostic value of FDG-PET response after chemoradiotherapy has not been definitively established (29, 30).

There were several limitations in this study. First, one critical step in quantifying DCE MRI parameters is to sample AIF from a major artery. However, to sample AIF in esophageal images can be challenging, because it’s complexity and typically small. Li et al. showed automatically sampling AIF by utilizing temporal and spatial features in a multistep interleaved manner, that highly resembled those manually sampled ones in leg arteries (31). Second, limited sample size, the number of TRG1 in particular, may lead to bias. Finally, GRASP reconstruction required offline reconstruction, more computing ability and more time for reconstruction.

Conclusions

Several pharmacokinetic parameters of DCE-MRI reconstructed by GRASP and VS-GR show significant differences between TRGs and response groups and thus can be used to non-invasively predict tumor response. GRASP may be better able to differentiate among these groups owing to its better temporal resolution.

Abbreviations

DCE-MRI dynamic contrast-enhanced Magnetic resonance imaging
GRASP golden-angle radial sparse parallel
VS-GR view-sharing with golden-angle radial profile
nCT neoadjuvant chemotherapy
EC esophageal cancer
TRG Tumor Regression Grade
AIF arterial input function
ROI regions of interest
Ktrans volume transfer constant
Kep rate contrast
Ve extravascular extracellular volume fraction
Vp plasma volume fraction
AUC the initial area-under-the- concentration versus time curve.

Declarations

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Availability of data and materials
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Authors’ contributions

Guarantors of integrity of entire study, J.Qu.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, Y.L., L.M., J.Qin., J.Qu.; clinical studies, Y.L., L.M., Z.W., J.G., H.Z., X.Y., H.L., J.Qin, J.Qu.; statistical analysis, Y.Zhao.; and manuscript editing, Y.L., L.M., J.Qin, J.Qu
Ethics approval and consent to participate
The study protocol was approved by institutional review board, and written informed consent was obtained from all participants.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

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Table 1: Details of reconstruction setting for radial VIBE with golden angle stack-of-stars sampling scheme

|                                | View-Sharing   | GRASP          |
|--------------------------------|----------------|----------------|
| number of acquired views       | 1659           |                |
| FOV                            | 300mm×300mm×146mm |                |
| spatial resolution             | 1.0×1.0×3.0 mm³ |                |
| temporal resolution            | 2.4 s/21.7s    | 4.5s           |
| number of dynamic volumes      | 68             | 68             |
| Reconstruction mode            | Online         | Offline        |
| Reconstruction time            | N/A            | 62 minutes on a CPU server |

Note: The temporal resolution of VS-GR means the starting time interval between two phases, however, 90% of the prior phase was overlapped with this phase. So, although the temporal resolution of VS-GR seems very short, actually it is longer.
Table 2 Patients’ information and TRG
| Study population          |         |
|--------------------------|---------|
| **Gender**               |         |
| Male                     | 52      |
| Female                   | 12      |
| **Age, years**           | 59.1±7.9|
| **Clinical T-stage**     |         |
| T1                       | 2       |
| T2                       | 15      |
| T3                       | 42      |
| T4                       | 5       |
| **Clinical N-stage**     |         |
| No                       | 32      |
| N1                       | 15      |
| N2                       | 15      |
| N3                       | 2       |
| **Type**                 |         |
| SCC                      | 59      |
| AC                       | 2       |
| ASC                      | 3       |
| **Tumor Regression Grade** |     |
| 1                        | 4       |
| 2                        | 4       |
| 3                        | 7       |
| 4                        | 11      |
| 5                        | 38      |
Table 3 Differences among TRG1-5 for DCE-MRI parameters with VS-GR and GRASP reconstruction.

| parameters | VS-GR reconstruction | GRASP reconstruction |
|------------|-----------------------|-----------------------|
|            | TRG 1 | TRG 2 | TRG 3 | TRG 4 | TRG 5 | c² | P value | TRG 1 | TRG 2 | TRG 3 | TRG 4 | TRG 5 | c² | P value |
| Kt ra m    | 0.00  | 1.07  | 0.71  | 2.47  | 2.39  | 20.1 | 0.00   | 0.00  | 0.15  | 0.17  | 0.32  | 0.31  | 15.5 | 0.00   |
| vs-GR      | 0.00  | 0.27  | 0.18  | 0.23  | 0.31  | 12.3 | 0.01   | 0.00  | 0.05  | 0.04  | 0.06  | 0.07  | 13.4 | 0.00   |
|            | 0.00  | 0.35  | 0.30  | 0.37  | 0.42  | 12.3 | 0.01   | 0.00  | 0.08  | 0.05  | 0.07  | 0.09  | 12.5 | 0.01   |
|            | 0.00  | 3.13  | 2.20  | 4.50  | 4.86  | 16.6 | 0.00   | 0.00  | 0.81  | 0.92  | 1.54  | 1.39  | 14.4 | 0.00   |
| Ke pm ax   | 0.00  | 1.08  | 0.36  | 0.53  | 0.89  | 15.2 | 0.00   | 0.00  | 0.29  | 0.21  | 0.27  | 0.33  | 10.3 | 0.03   |
|            | 0.00  | 0.72  | 0.21  | 0.34  | 0.53  | 15.0 | 0.00   | 0.00  | 0.29  | 0.21  | 0.27  | 0.33  | 10.3 | 0.03   |
| Ve pm %    | 1.00  | 1.00  | 1.00  | 1.00  | 7.18  | 0.12 | 1.00   | 0.82  | 1.00  | 1.00  | 1.00  | 3.44  | 0.48 |        |

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|           | 0.5  | 1.0  | 1.0  | 1.0  | 1.0  | 1.0  | 1.0  | 0.3  | 0.4  | 1.0  | 0.8  |
|-----------|------|------|------|------|------|------|------|------|------|------|------|
| Ve mean   | 0.00 | 0.34 | 0.36 | 0.33 | 0.31 | 11.5 | 0.02 | 0.00 | 0.19 | 0.18 | 0.23 | 0.23 |
| Ve 75%    | 0.00 | 0.38 | 0.50 | 0.50 | 0.46 | 11.4 | 0.02 | 0.00 | 0.22 | 0.21 | 0.25 | 0.25 |
| Vp mean   | 0.00 | 0.06 | 0.05 | 0.24 | 0.14 | 14.1 | 0.00 | 0.00 | 0.06 | 0.08 | 0.20 | 0.13 |
| Vp 75%    | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 9.77 | 0.04 | 0.00 | 0.00 | 0.00 | 0.01 | 0.01 |
| AU C max  | 0.00 | 0.07 | 0.08 | 0.10 | 0.12 | 21.3 | 0.00 | 0.00 | 1.73 | 3.34 | 4.56 | 3.36 |
| AU C mean | 0.00 | 0.03 | 0.04 | 0.36 | 0.04 | 11.4 | 0.02 | 0.00 | 0.94 | 1.47 | 1.68 | 1.53 |
| AU C 75%  | 0.00 | 0.04 | 0.05 | 0.05 | 0.05 | 11.9 | 0.01 | 0.00 | 1.18 | 1.64 | 2.04 | 1.85 |

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Note. — Data are median (P25, P75).

Table 4 Differences between responder and non-responder groups for DCE-MRI parameters with VS-GR/GRASP reconstruction.

| Parameter  | VS-GR reconstruction |  |  |  |  |  |  |  |  |
|------------|-----------------------|---|---|---|---|---|---|---|---|
|            | responder | non-responder | U  | P value | responder | non-responder | U  | P value |
| Ktrans max | 0.314     | 2.303       | 51.0 | 0.001   | 0.101     | 0.304       | 69.0 | 0.002   |
|            | (0.000,1.097) | (1.172,3.564) |     |         | (0.000,0.189) | (0.196,0.415) |     |         |
| Ktrans mean| 0.055     | 0.299       | 92.0 | 0.007   | 0.031     | 0.065       | 104.0 | 0.015   |
|            | (0.000,0.298) | (0.157,0.387) |     |         | (0.000,0.067) | (0.046,0.094) |     |         |
| Ktrans 75% | 0.069     | 0.404       | 92.0 | 0.007   | 0.043     | 0.082       | 115.0 | 0.027   |
|            | (0.000,0.395) | (0.200,0.545) |     |         | (0.000,0.097) | (0.061,0.121) |     |         |
| Kep max    | 1.088     | 4.272       | 90.0 | 0.007   | 0.559     | 1.342       | 75.0  | 0.002   |
|            | (0.000,3.309) | (2.307,6.527) |     |         | (0.000,0.934) | (0.861,1.875) |     |         |
| Kep mean   | 0.149     | 0.506       | 140.0 | 0.088   | 0.160     | 0.318       | 117.0 | 0.030   |
|            | (0.000,0.751) | (0.251,0.823) |     |         | (0.000,0.340) | (0.212,0.432) |     |         |
|                  | Kep 75% | Ve max | Ve mean | Ve 75% | Vp max | Vp mean | Vp 75% | AUC max | AUC mean | AUC 75% |
|------------------|---------|--------|---------|--------|--------|---------|--------|---------|---------|---------|
|                  | 0.384   | 1.000  | 0.030   | 0.006  | 0.017  | 0.004   | 0.001  | 0.050   | 0.016   | 0.020   |
|                  | (0.000,1.095) | (1.000,1.00) | (0.000,0.388) | (0.000,0.471) | (0.000,0.068) | (0.0000,0.0048) | (0.001,0.001) | (0.000,0.001) | (0.000,0.001) | (0.000,0.001) |
|                  | 0.772   | 1.000  | 0.323   | 0.475  | 0.140  | 0.002   | 0.001  | 0.108   | 0.039   | 0.052   |
|                  | (0.363,1.334) | (1.000,1.00) | (0.201,0.370) | (0.297,0.521) | (0.056,0.316) | (0.001,0.006) | (0.001,0.001) | (0.085,0.233) | (0.030,0.047) | (0.052,0.047) |
|                  | 154.0   | 199.5  | 124.0   | 112.0  | 71.0   | 135.0   | 142.0  | 40.0    | 90.0    | 86.0    |
|                  | (0.000,0.509) | (0.736,1.000) | (0.000,0.207) | (0.000,0.250) | (0.000,0.70) | (0.000,0.009) | (0.000,0.012) | (2.489,4.832) | (1.188,1.901) | (1.403,2.203) |
|                  | 0.155   | 0.099  | 0.042   | 0.023  | 0.002  | 0.071   | 0.096  | 0.001   | 0.007   | 0.005   |
|                  | (0.268,0.536) | (0.875,1.000) | (0.189,0.276) | (0.209,0.311) | (0.085,0.233) | (0.008,0.030) | (0.008,0.042) | (1.188,1.901) | (1.188,1.901) | (1.403,2.203) |
|                  | 0.215   | 1.000  | 0.163   | 0.187  | 0.046  | 0.001   | 0.001  | 1.062   | 0.569   | 0.753   |
|                  | (0.000,0.509) | (0.875,1.000) | (0.000,0.207) | (0.000,0.250) | (0.000,0.70) | (0.000,0.009) | (0.000,0.012) | (2.489,4.832) | (1.188,1.901) | (1.403,2.203) |
|                  | 0.429   | 1.000  | 0.227   | 0.250  | 0.133  | 0.014   | 0.023  | 3.424   | 1.515   | 1.854   |
|                  | (0.268,0.536) | (0.875,1.000) | (0.000,0.207) | (0.000,0.250) | (0.000,0.70) | (0.000,0.009) | (0.000,0.012) | (2.489,4.832) | (1.188,1.901) | (1.403,2.203) |
|                  | 137.0   | 223.0  | 93.0    | 104.0  | 63.0   | 67.0    | 65.0   | 31.0    | 60.0    | 55.0    |
|                  | (0.000,0.509) | (0.875,1.000) | (0.000,0.207) | (0.000,0.250) | (0.000,0.70) | (0.000,0.009) | (0.000,0.012) | (2.489,4.832) | (1.188,1.901) | (1.403,2.203) |
|                  | 0.077   | 0.979  | 0.008   | 0.015  | 0.001  | 0.001   | 0.001  | 0.001   | 0.001   | 0.001   |

Note. —Data are median (P25, P75).
Table 5 DCE-MRI parameters with VS-GR/GRASP stratified according to TRGs and response.
| Parameters       | TRG1-5 | responder and non-responder |
|------------------|--------|-----------------------------|
|                  |        | VS-GR | GRASP | VS-GR | GRASP |
|                  |        | $r^*(P)$ | $r^*(P)$ | $r^*(P)$ | $r^*(P)$ |
| Ktrans max       | 0.409(0.001) | 0.343(0.006) | 0.443(<0.001) | 0.396(0.001) |
| Ktrans mean      | 0.305(0.014) | 0.320(0.010) | 0.338(0.006) | 0.307(0.014) |
| Ktrans 75%       | 0.318(0.011) | 0.282(0.024) | 0.338(0.006) | 0.279(0.026) |
| Kep max          | 0.379(0.002) | 0.323(0.009) | 0.343(0.006) | 0.381(0.002) |
| Kep mean         | 0.314(0.012) | 0.255(0.042) | 0.215(0.088) | 0.274(0.029) |
| Kep 75%          | 0.283(0.023) | 0.238(0.058) | 0.179(0.157) | 0.223(0.077) |
| Ve max           | 0.097(0.446) | -0.035(0.784) | 0.208(0.099) | -0.003(0.979) |
| Ve mean          | 0.125(0.324) | 0.318(0.010) | 0.256(0.041) | 0.335(0.007) |
| Ve 75%           | 0.151(0.234) | 0.330(0.008) | 0.286(0.022) | 0.307(0.014) |
| Vp max           | 0.312(0.012) | 0.333(0.007) | 0.391(0.001) | 0.412(0.001) |
| Vp mean          | 0.158(0.213) | 0.371(0.003) | 0.228(0.070) | 0.402(0.001) |
| Vp 75%           | 0.115(0.366) | 0.370(0.003) | 0.210(0.096) | 0.407(0.001) |
| AUC max          | 0.524(<0.001) | 0.253(0.044) | 0.471(<0.001) | 0.494(<0.001) |
| AUC mean         | 0.294(0.018) | 0.306(0.014) | 0.343(0.006) | 0.419(0.001) |
| AUC 75%          | 0.314(0.012) | 0.307(0.014) | 0.353(0.004) | 0.432(<0.001) |

Note.—$r^*$ is the Spearman correlation coefficient obtained from the nonparametric Spearman correlation test.
Figures

Figure 1
Flow chart illustrates patient selection process for study cohort.

Figure 2
Arterial contrast concentration curve from GRASP (red) and view-sharing (blue) reconstruction using the same dynamic acquisition. GRASP’s AIF is closer to the true AIF with steeper slope and sharp peak than view-sharing.