



# OPEN Feasibility and comparison of 3D modified rosette ultra-short echo time (PETALUTE) with conventional weighted acquisition in $^{31}\text{P}$ -MRSI

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Phosphorus-31 magnetic resonance spectroscopic imaging ( $^{31}\text{P}$ -MRSI) provides valuable non-invasive information on tissue metabolism but is burdened by poor sensitivity and prolonged scan duration. Ultra-short echo time (UTE) acquisitions minimize signal loss when probing signals with relatively short spin-spin relaxation time ( $T_2$ ), while also preventing first-order dephasing. Here, a three-dimensional (3D) UTE sequence with a rosette k-space trajectory (PETALUTE) is applied to  $^{31}\text{P}$ -MRSI at 3T. Conventional weighted MRSI employs highly regular Cartesian k-space sampling, susceptible to substantial artifacts when accelerated via undersampling. In contrast, this novel sequence's "petal-like" pattern offers incoherent sampling more suitable for compressed sensing (CS). These results showcase the competitive performance of PETALUTE against conventional weighted  $^{31}\text{P}$ -MRSI with simulation, phantom, and in vivo leg muscle comparisons.

Phosphorous-31 magnetic resonance spectroscopy ( $^{31}\text{P}$ -MRS), the longest-standing in vivo MRS modality, can be an invaluable tool for probing in vivo metabolites such as phosphocreatine (PCr), inorganic phosphate (Pi), phosphomonoesters (PMEs), phosphodiester (PDEs), and adenosine triphosphate (ATP)<sup>1,2</sup>. As fundamental phospholipids and constituents of the high-energy phosphate pathway, these  $^{31}\text{P}$  metabolites provide noninvasive measures of tissue pH, lipid metabolism, and oxidative bioenergetics<sup>3,4</sup>. Thus  $^{31}\text{P}$ -MRS possesses versatile diagnostic and prognostic potential. For instance, elevated PME/PDE ratios and reduced ATP levels have been reported in diseased and cancerous liver tissue, often correlated with classical plasma markers and Child-Pugh scores<sup>5–9</sup>. Furthermore  $^{31}\text{P}$ -MRS has been used to assess whole-liver treatment efficacy, monitoring metabolite changes in malignant tissues following therapy<sup>10</sup>. Likewise, diminished PCr/ATP ratios and post-exercise PCr recovery rates have been measured in cardiac and skeletal muscles of patients with type 2 diabetes<sup>11</sup>. Numerous endeavors have employed  $^{31}\text{P}$ -MRS in the brain, heart, and muscle, seeking out alterations in neurodegenerative, cardiovascular, metabolic, and oncological diseases<sup>12–20</sup>.

While relevant  $^1\text{H}$ -MRS metabolites can be obscured by contaminating fat, water, and macromolecular background signals, widely spaced  $^{31}\text{P}$  spectral peaks are more easily elucidated due to the absence of these nuisance signals. However, in contrast to  $^1\text{H}$ -MRS  $^{31}\text{P}$ -MRS is burdened by a lower gyromagnetic ratio and relatively short spin-spin metabolite relaxation times ( $T_2$ );<sup>21,22</sup> these factors engender extremely poor in vivo

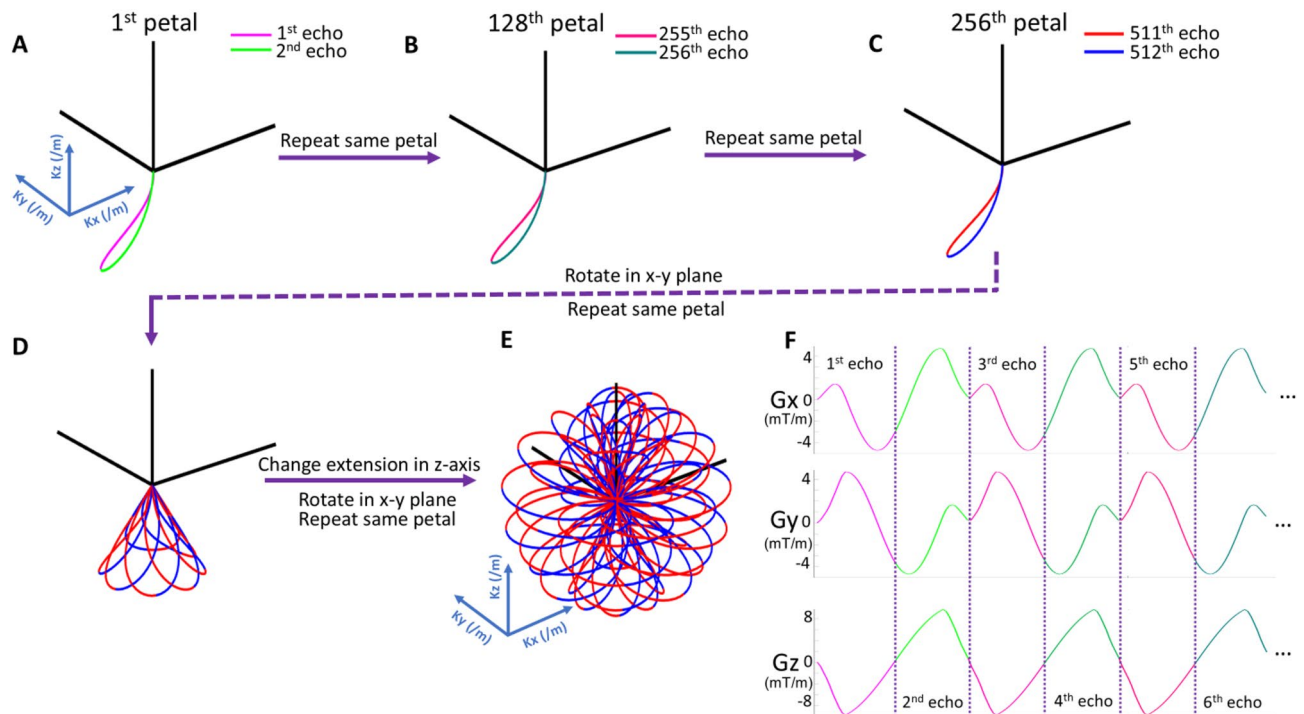
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relative sensitivity and force a delicate balance between SNR, resolution, and scan duration. Low  $^{31}\text{P}$ -MRS tissue concentrations (approximately 2 mM  $\gamma$ -ATP in liver<sup>23</sup>) further exacerbate SNR challenges, so that commonly used acquisition delays ( $T_E > 300\ \mu\text{s}$ ) with conventional methods result in prolonged acquisition, phase distortions, baseline roll, and subsequent operator errors during metabolite quantification. Such complications have been severely limiting factors in the clinical feasibility of  $^{31}\text{P}$ -MRS. Recent advances in coil engineering and the introduction of ultra-high field (UHF,  $B_0 > 3\text{T}$ ) scanners have assisted in mitigating these limiting factors; one experiment demonstrated a 2.8-factor increase in PCr SNR at 7T relative to 3T<sup>24</sup>. Conversely, UHF acquisitions also necessitate larger spectral bandwidth (SBW), with a 40-ppm range requiring approximately 2.0 kHz at 3T but 4.8 kHz at 7T. Still, excessive acquisition durations remain the clear barrier to clinical translation without innovative acceleration.

To address these points, we propose a novel three-dimensional (3D), ultra-short echo time (UTE) sequence with a rosette<sup>25</sup> k-space trajectory (PETALUTE, previously validated in ultra-short- $T_2$  imaging<sup>26,27</sup>, brain iron mapping<sup>28,29</sup>, and sodium quantification<sup>30</sup>) for  $^{31}\text{P}$  magnetic resonance spectroscopic imaging (MRSI)<sup>31</sup>. Compared to conventional Cartesian MRSI k-space trajectories, rosette's "petal-like" pattern (Fig. 1) maps 3D k-space far more efficiently. Additionally, rosette's relatively incoherent data sampling allows the possibility of significant acceleration through higher undersampling factors and compressed sensing (CS) reconstruction; offering better k-space coverage when compared to radial and spiral trajectories, generalized rosette's curvature affords superior SNR performance under aggressive acceleration<sup>32</sup>. Furthermore, the rosette's center-out k-space design enables UTE acquisition, thereby permitting capture of short- $T_2$  signals before significant transverse signal decay and first-order dephasing occur; this enhances SNR, simplifies spectral pre-processing, and minimizes operator-dependent quantification errors.

Substantial efforts have been invested towards clinically feasible  $^{31}\text{P}$ -MRSI, experimenting with short repetition times ( $T_R$ ), measuring multiple k-space points per  $T_R$ , k-space undersampling, enhancing reconstruction via prior knowledge, and their conceivable combinations<sup>33</sup>. 3D extensions of ISIS have shown promise in UHF preclinical and 3T cardiac studies but remain limited by time resolution and motion artifact sensitivity<sup>34,35</sup>. Non-localized or FID acquisitions are often preferred to minimize rapid  $^{31}\text{P}$  metabolite  $T_2$ -decay, but also to overcome specific absorption rate (SAR) limitations at UHFs. Thus, variations of spatial-spectral encoding (SSE) schemes and their synergies with k-space undersampling appear to be the more promising avenue forward; several Cartesian and non-Cartesian acquisition designs offer varying degrees of SNR efficiency, k-space weighting, gradient system demands, and undersampling acceleration potential.

For example, flyback and multishot EPSI have been tested in brain<sup>36,37</sup> and skeletal calf muscle<sup>38</sup>, offering considerable time savings over conventional phase encoding when combined with CS acceleration;<sup>39</sup> despite its acceleration potential, EPSI<sup>36,40–42</sup> offers lower SNR efficiency and SBW at fine resolutions than other SSE



**Fig. 1.** Illustration of 3D rosette k-space trajectory and gradients. (A)–(C) Acquisition begins at k-space center for every petal, crossing k-space origin twice at each petal's beginning and end. Petals can be manually separated into two halves, similar to odd and even echoes in EPSI MRSI. (D,E) Varied petal rotations form the rosette pattern, providing sufficient k-space coverage. (F) With the closed-loop trajectory, acquisition delay is further minimized by enabling the analog to digital converter (ADC) for sampling during gradient ramp-up.

options. Density-weighted concentric ring<sup>43,44</sup> trajectories (CRTs) grant increased SNR efficiency and SBW limits, enabling faster MRSI even with UHF systems. CRTs boast flexibility in weighting and temporal interleaves, allowing tailoring according to acceleration needs and gradient slew rates. Similarly, spiral-encoded<sup>45</sup><sup>31</sup>P-MRSI has exhibited faster dynamic calf muscle mapping than conventional elliptical phase-encoded acquisition<sup>46</sup>. Though spirals offer high acceleration, SNR efficiency, and customizable weighting, they are also limited by SBW and gradient system hardware.

Conventional MRSI FIDs commonly possess  $T_E$  on the order of 1–2 ms, restricted by the duration of constant excitation pulses and phase encoding gradients to reach the outermost k-space points. This acquisition delay can be decreased using variable pulse widths and amplitudes. Sampling throughout gradient transition periods, or ramp sampling, remains an additional option for minimizing  $T_E$ . Studies have demonstrated  $T_E$  as low as 480  $\mu$ s and 520  $\mu$ s for EPSI and radial EPSI, respectively<sup>39,47</sup>. Acquisitions using such UTE-MRSI techniques<sup>48</sup> have achieved  $T_E = 300 \mu$ s at 3T and  $T_E = 500 \mu$ s at 7T<sup>49,50</sup>. In non-Cartesian center-out k-space trajectories employing ramp sampling,  $T_E$  is primarily limited by the dead time between coil transmit-receive switching, permitting the shortest possible  $T_E$ . Despite this possibility, SBW constraints and conventional sequence parameter ( $T_A$ /FOV) matching have prevented extensive investigation of non-Cartesian UTE <sup>31</sup>P-MRSI.

In this study, we evaluate the PETALUTE <sup>31</sup>P-MRSI with a novel rosette k-space trajectory by comparing its performance to conventional 3D weighted Cartesian <sup>31</sup>P-MRSI in the quadriceps muscle at 3T. We ultimately aim to demonstrate its potential value in clinical spectroscopic acquisitions.

Methods  
k-space trajectory designs for MRSI

PETALUTE

General sequence parameters were as follows:  $T_A = 36:00$ ,  $T_R = 350$  ms,  $T_E = 65 \mu$ s, matrix size ( $N_x \times N_y \times N_z$ ) =  $24 \times 24 \times 24$ , nominal voxel size = 8 mL, FOV =  $480 \times 480 \times 480$  mm<sup>3</sup>, SBW = 2083 Hz, time samples = 512. Parameters are summarized in Table 1.

As in prior work<sup>26</sup>, 3D PETALUTE k-space trajectory (Fig. 1) for <sup>31</sup>P-MRSI was generated with Eqs. (1) and (2):

$$K_{xy} = Kx(t) + iKy(t) \\ = (K \max * \cos(\varphi)) \sin(\omega_1 t) e^{i\omega_2 t + \beta} \tag{1}$$

$$K_z(t) = (K \max * \sin(\varphi)) \sin(\omega_1 t) \tag{2}$$

Where  $K \max$  is the furthest distance in k-space (=25 cycle/m in this study), the radial direction oscillation frequency ( $\omega_1$ ) and the angular direction oscillation frequency ( $\omega_2$ ) were set equally ( $\omega_1 = \omega_2$ ),  $\phi$  determines the z-axis location, which was sampled uniformly in the range of  $[-\pi/2, \pi/2]$ , and  $\beta$  determines the initial angular direction phase, which was sampled uniformly in the range of  $[0, 2\pi]$ .

$$K \max = \frac{N_x}{2 * \text{FOV}} = 25 \text{ cycle/m}$$

Other imaging parameters included: hard rectangular RF pulse duration = 50  $\mu$ s, flip angle  $\alpha = 20^\circ$ , dwell time  $\Delta t = 5 \mu$ s in the readout, and each rosette petal designed with  $N_{pp} = 96$  points. This leads to

$$\text{SBW} = \frac{1}{N_{pp} * \Delta t} = (480 \mu \text{s})^{-1} = 2083 \text{ Hz}$$

as well as

|                        | PETALUTE   | Weighted MRSI |
|------------------------|------------|---------------|
| $T_A$ (mm: ss)         | 36:00      | 36:56         |
| $T_R$                  | 350 ms     | 1000 ms       |
| $T_E$                  | 70 $\mu$ s | 2.3 ms        |
| $\alpha$               | 20°        | 90°           |
| Number of averages     | 4          | 4             |
| Reconstruction matrix  | 24         | 16            |
| Nominal voxel (mL)     | 8          | 8             |
| FOV (mm <sup>3</sup> ) | 480        | 320           |
| Bandwidth (Hz)         | 2083       | 2200          |
| Time samples           | 512        | 512           |
| $T_A$ relative to MRSI | 0.97       | 1.00          |

**Table 1.** Table of protocol parameters for conventional 3D weighted MRSI and novel PETALUTE MRSI acquisitions. Nominal voxel size was matched between methods, with total acquisition time approximately equal between the two sequences. SBWs were matched via interpolation during post-processing.

$$\omega_1 = \omega_2 = \pi * \text{SBW} = 6545 \text{ rad/s}$$

and the resulting  $-20$  to  $+20$  ppm in the 3T spectral range is more than sufficient for  $^{31}\text{P}$ -MRS. In reconstruction, each petal was downsampled to  $N_{pp} = 48$  by averaging the oversampled points. With a matrix size of  $24 \times 24 \times 24$  for the reconstruction, the required number of petals ( $N_p$ ) to satisfy Nyquist criterion was calculated as

$$N_p = 4\pi * \left(\frac{N_x}{2}\right)^2 \approx 1810$$

However, due to the rosette's efficient sampling scheme, only 79.8% coverage (i.e.,  $N_p = 1444$ ) was defined as full k-space acquisition. Thus, the acquisition time per average was calculated as

$$T_A = N_p * T_R = 505 \text{ s}$$

or roughly 9 min. A complete description including the influence of trajectory parameters, Nyquist criterion, and the specific gradient ramp-up of this 3D rosette k-space pattern is provided in earlier work (Shen et al.)<sup>26</sup>.

#### Conventional weighted MRSI

Conventional Cartesian 3D acquisitions used the vendor-provided  $^{31}\text{P}$ -MRSI FID with k-space weighting and Hanning filter. Sequence parameters were as follows:  $T_A = 36:56$ ,  $T_R = 1000$  ms,  $T_E = 2.3$  ms, matrix size ( $N_x \times N_y \times N_z$ ) =  $16 \times 16 \times 16$ , nominal voxel size = 8 mL, FOV =  $320 \times 320 \times 320$  mm<sup>3</sup>, SBW = 2200 Hz, time samples = 512. The acquisition used the vendor H-Sinc excitation pulse with 1.28 ms duration and  $\alpha = 90^\circ$ .

Parameters are summarized in Table 1.

#### Simulations

To assess the theoretical performance of the PETALUTE relative to conventional weighted MRSI, MATLAB (MathWorks, Natick, USA) simulations were run examining side lobes and SNR relative to the spatial response function (SRF). A simple, constant 3D object was placed at the origin of a  $48 \times 48 \times 48$  grid (FOV = 480 mm isotropic producing a nominal voxel size = 1 mL) and reconstructed using the non-uniform FFT (NUFFT) method<sup>51</sup> and k-space information for each in vivo acquisition. We discuss both SRF and point spread function (PSF) since the former specifically estimates side lobes and signal bleed between adjacent voxels, while the latter measures contribution from a single object point to the entire population of voxels.

#### Experimental comparison

All data acquisition occurred on a 3T MRI system (Prisma, Siemens, Erlangen, Germany) with  $G_{\text{max}} = 80$  mT/m and slew rate = 200 mT/m/ms isotropic. This study conforms to the Declaration of Helsinki, with all protocols approved and conducted in accordance with the Institutional Review Boards of Purdue University. Written informed consent was obtained from all human subjects.

The rosette and conventional acquisitions were tested with a uniform 2-liter bottle phantom (0.17 mg/mL phosphoric acid) using a dual-tuned  $^1\text{H}/^{31}\text{P}$  Tx/Rx flexible 11-cm surface coil (RAPID Biomedical). For in vivo comparison, five healthy volunteers (BMI =  $26 \pm 2$  kg/m<sup>2</sup>; age =  $29 \pm 5$  years; 2 f / 3 m) received leg scans with an 8-channel, dual-tuned  $^1\text{H}/^{31}\text{P}$  Tx/Rx phased array coil<sup>52</sup> (Stark Contrast, Erlangen, Germany). Quadriceps was chosen for its superior PCr SNR and absence of respiratory motion during prolonged scanning. Subjects were positioned feet-first and supine, with the upper quadriceps tightly surrounded by the coil plates. Following localizer imaging, the adjustment volume was manually positioned (spanning both legs), and linewidth was minimized using a 3D GRE field map and interactive Siemens shimming. Each subject was scanned first with the conventional weighted Cartesian acquisition followed uninterrupted by the PETALUTE  $^{31}\text{P}$ -MRSI.

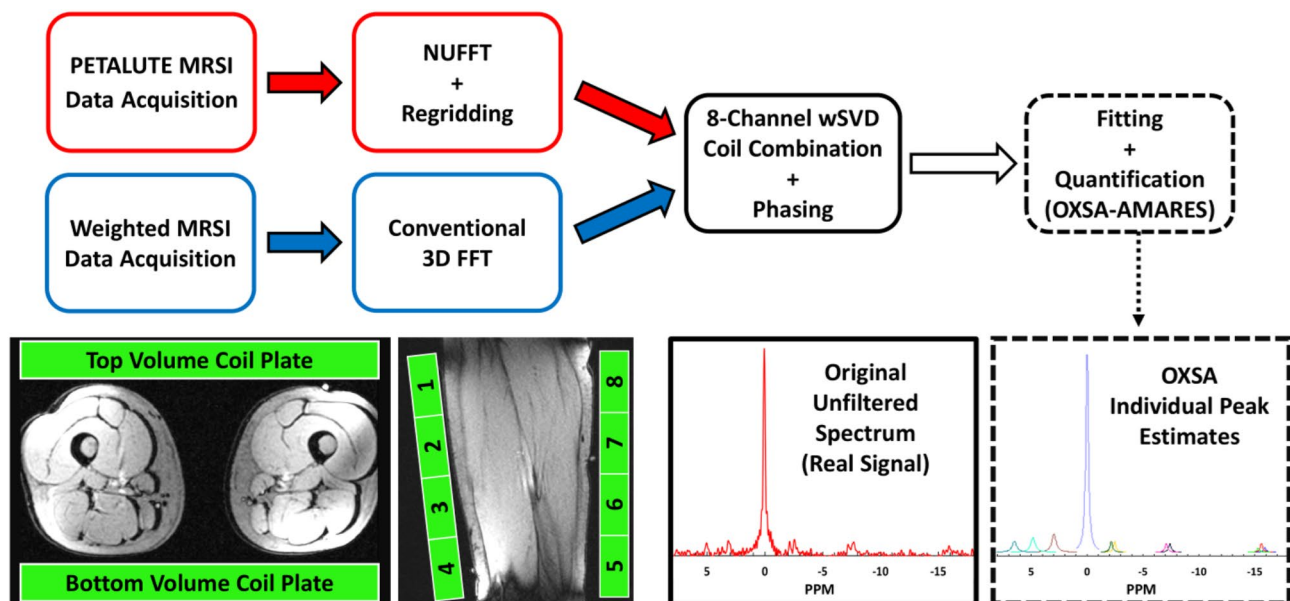
#### Post-processing and reconstruction

Raw data files were exported for reconstruction and pre-processing in MATLAB. Gridding and FFT were completed using adjoint, type 2 (forward) NUFFT regridding<sup>53</sup> and density compensation according to the Pipe method<sup>54</sup>. Data were Hanning filtered and, when necessary, coil-combined using whitened singular value decomposition (wSVD) with the noise covariance matrix ( $\Sigma$ ) approximated from spectral regions without signal<sup>55</sup>. Spectra from the PETALUTE were zero-order phased by maximizing the integral of the largest peak (PCr, 0 ppm). Spectra from the conventional weighted MRSI were both zero-order phased and first-order phased to correct a 2.3-ms delay.

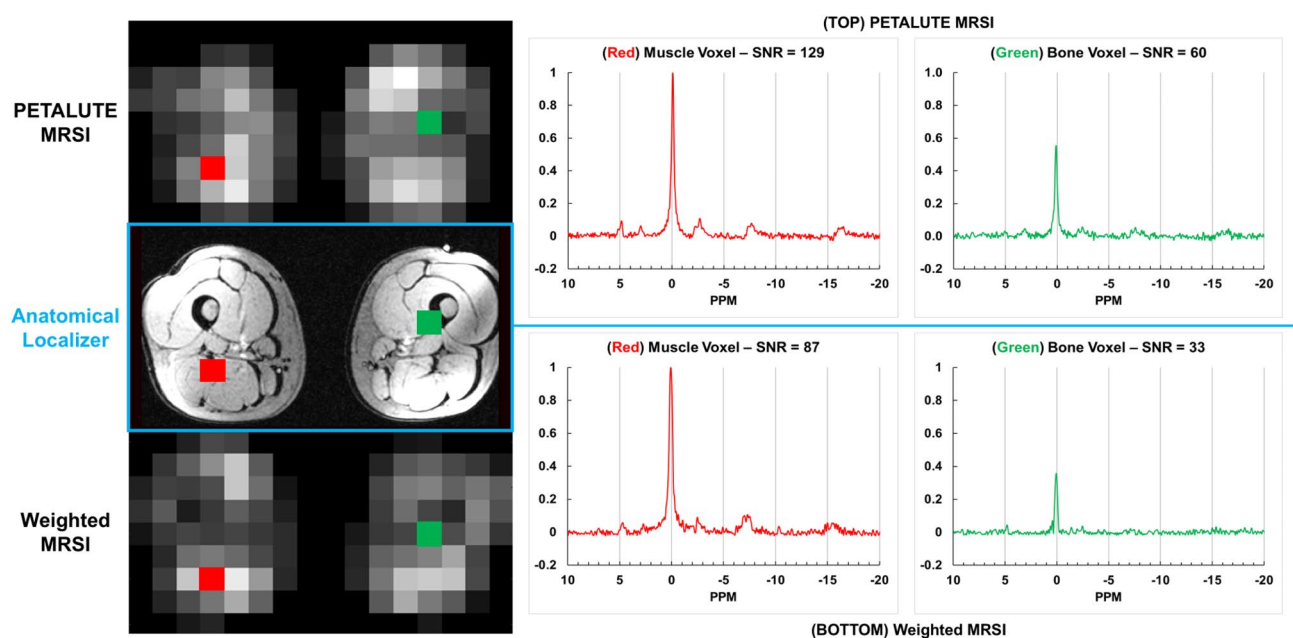
#### SNR and quantification

Spectra were fitted within the Oxford Spectroscopy Analysis (OXSA) toolbox<sup>56</sup> using AMARES methods. Metabolite peak SNRs were calculated from real-valued spectra according to Eq. (3), with noise variance calculated from a residual region lacking metabolite signals. As an additional signal quantification metric, "raw SNR" (Eq. (4)) was estimated by dividing the highest absolute-value peak point by the noise variance in an off-spectrum region; this method carries the advantage of consistently assessing signal strength regardless of any interfering spectral phase.

$$\text{SNR}_{\text{OXSA}} = \frac{\text{Peak Signal Fit (Real)}}{\text{RMS}_{\text{residual noise}}} \quad (3)$$



**Fig. 2.** Workflow of data acquisition, reconstruction, processing, and analysis. Subjects were positioned feet-first supine with both quadriceps positioned between the 30-cm phased array coil plates. Raw data were exported, appropriately reconstructed, coil-combined, and phased prior to fitting and quantification.



**Fig. 3.** (A) Signal intensity and selected central axial slices for Subject 3's PETALUTE acquisition. (B) Visualization of "raw SNR" calculation on  $^{31}\text{P}$ -MRS muscle spectrum in one voxel. (C) Results for quantifiable ( $\text{SNR} > 3$ ) voxels within selection.

$$\text{SNR}_{\text{raw}} = \frac{\text{Maximum Absolute Peak Amplitude}}{\text{RMS}_{\text{off-spectrum noise}}} \quad (4)$$

Figures 2 and 3 summarize data acquisition, reconstruction, processing, and analysis workflow.

### Quantitative analysis

The performance of PETALUTE and weighted MRSI in phantom solution and quadriceps muscle were assessed using Pi and PCr metabolite signals, respectively. Quantification considered the central, highest signal axial slices within each subject, attempting to quantify every voxel. Only voxels with  $\text{SNR} > 3$  and OXSA-AMARES

Cramér-Rao lower bound (CRLB) goodness of fit smaller than 20% for PCr peak were included in the final analysis. The statistical significance of SNR results was assessed using right-tailed Welch's t-tests.

## Results

### Spatial response function simulation comparison of PETALUTE with weighted MRSI

The impact of varying k-space sampling trajectories on image quality can be evaluated via SRF simulations as shown in Fig. 4. FWHMs along the x-axis at the center of the FOV were comparable between rosette (30.7 mm) and weighted MRSI (36.1 mm). Both acquisition schemes exhibit noticeable sidelobe noise, albeit with slightly reduced side lobes in the rosette trajectory close to the object origin.

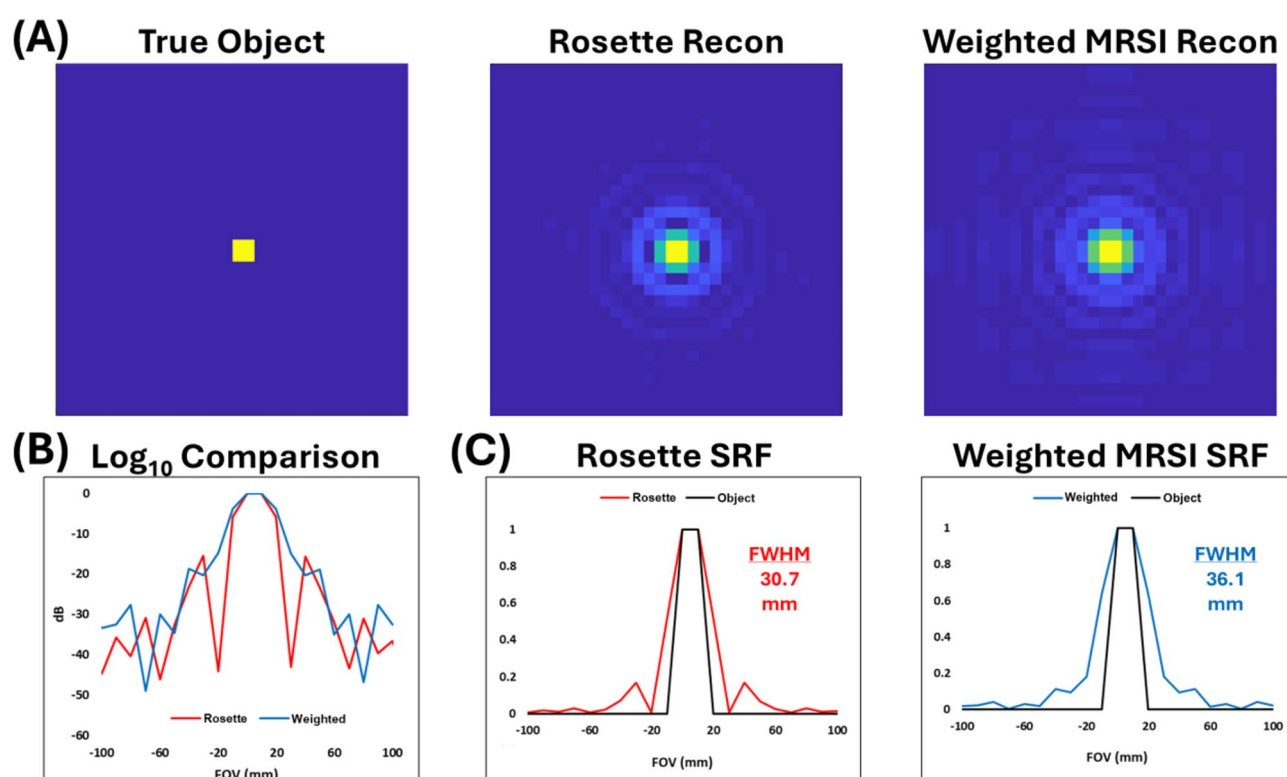
### Phantom comparison of PETALUTE with weighted MRSI

Figure 5 presents results and setup of phantom experiments with dual-tuned flexible surface coil. With approximately matched acquisition times, mean raw SNR (Eq. 4) was 69% higher in PETALUTE than in weighted MRSI. Spectral linewidth was approximately identical between the two acquisitions. Right-tailed t-test confirmed the statistical significance of rosette's SNR advantage ( $p < 0.001$ ).

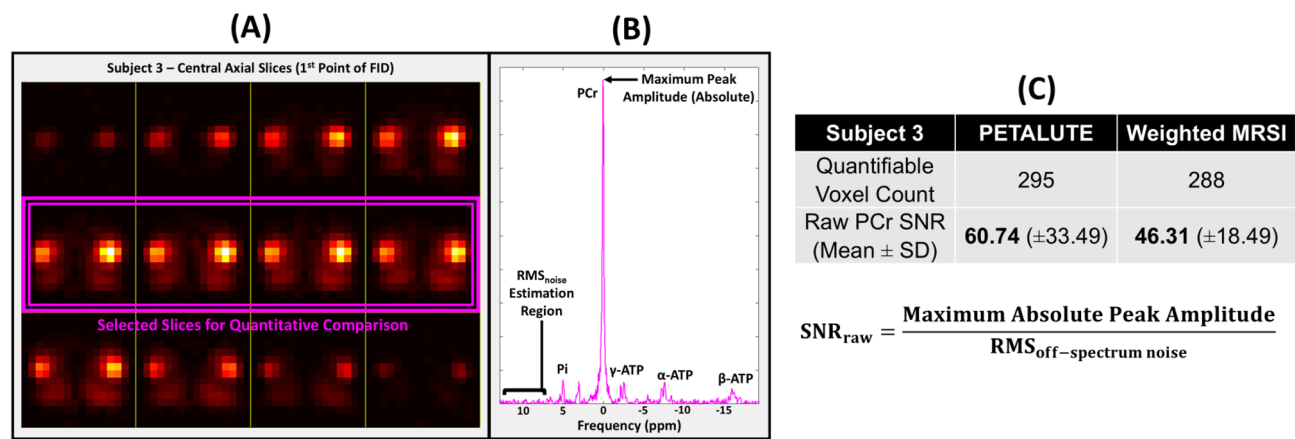
### In vivo leg comparison of PETALUTE with weighted MRSI

Figure 6 shows representative PETALUTE and weighted MRSI axial PCr maps and spectra in the same volunteer. High-signal muscle regions are clearly distinguishable from low-signal bony femur regions. As expected, PCr predominates the  $^{31}\text{P}$  muscle spectrum alongside smaller Pi and ATP peaks.

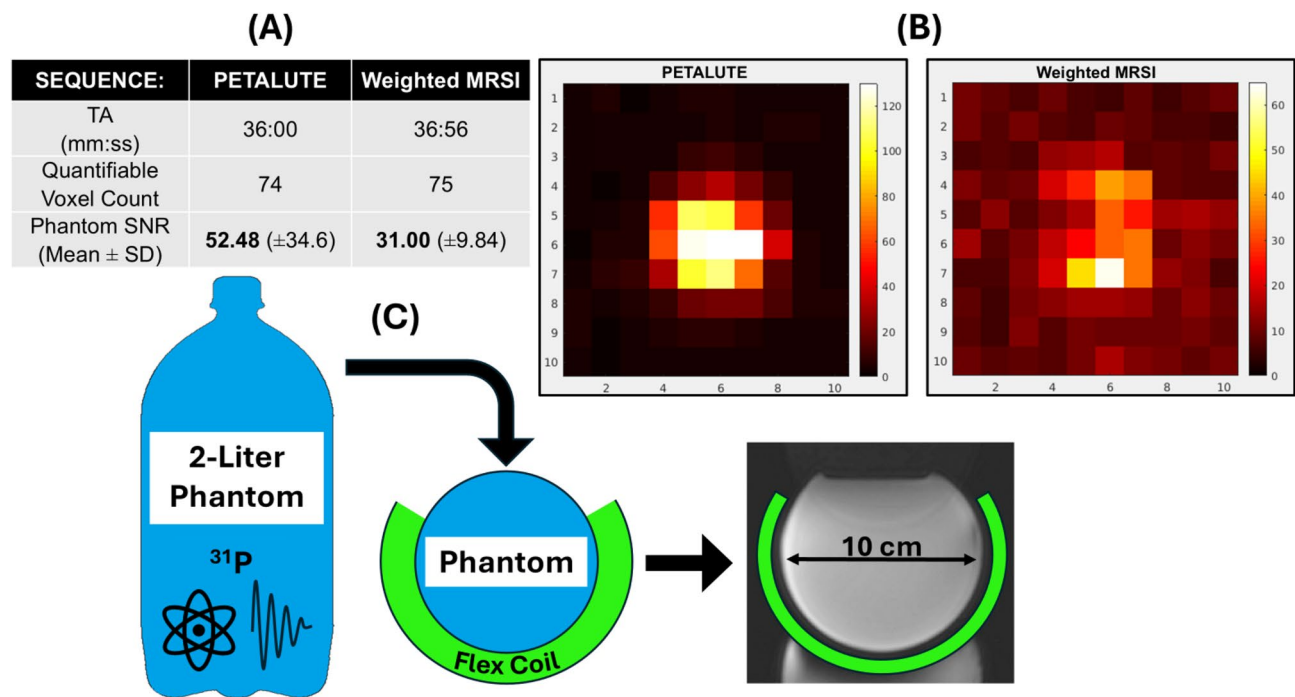
Figure 7 provides the quantitative PCr results for all subjects, illustrating the different SNRs obtained from Eqs. (3) and (4), respectively. Tables 2 and 3, and 4 summarize these distinctions. While PETALUTE consistently outperformed weighted MRSI, the advantage was slightly more prominent in AMARES-fitting of the real data at 34% compared to raw SNR of absolute data at 18%. CRLBs for quantified voxels (see Supplementary Table S1) were well below the 20% limit, with a mean below 3% in all subjects. PCr peak spectral linewidth was nearly matched between the two acquisitions (see Supplementary Table S2) with FWHMs around 4 Hz or below. Right-tailed t-tests confirm the statistical significance of PETALUTE's higher SNR in both cases ( $p < 0.001$ ).



**Fig. 4.** Results of spatial response function (SRF) simulation for novel 3D PETALUTE and conventional 3D weighted MRSI sequences. **(A)** 2D (xy-plane) SRFs for simulated object and each k-space trajectory at center of the FOV. **(B)** 1D (x-axis) log<sub>10</sub> decibel comparison between k-space trajectories at center of the FOV. **(C)** 1D (x-axis) comparisons between each normalized reconstruction and the true simulated object at center of the FOV.



**Fig. 5.** Results from phantom measurements using “raw SNR” (Eq. 4) of absolute inorganic phosphate (Pi) metabolite signal. (A) With approximately matched acquisition times, PETALUTE’s mean SNR was 69% higher. (B) As both sequences share the same nominal resolution, example axial SNR maps show clear signal intensity across a width of 5 voxels (equivalent to 100 mm). (C) A uniform 100-mm diameter Pi bottle phantom was prepared and used for both measurements.

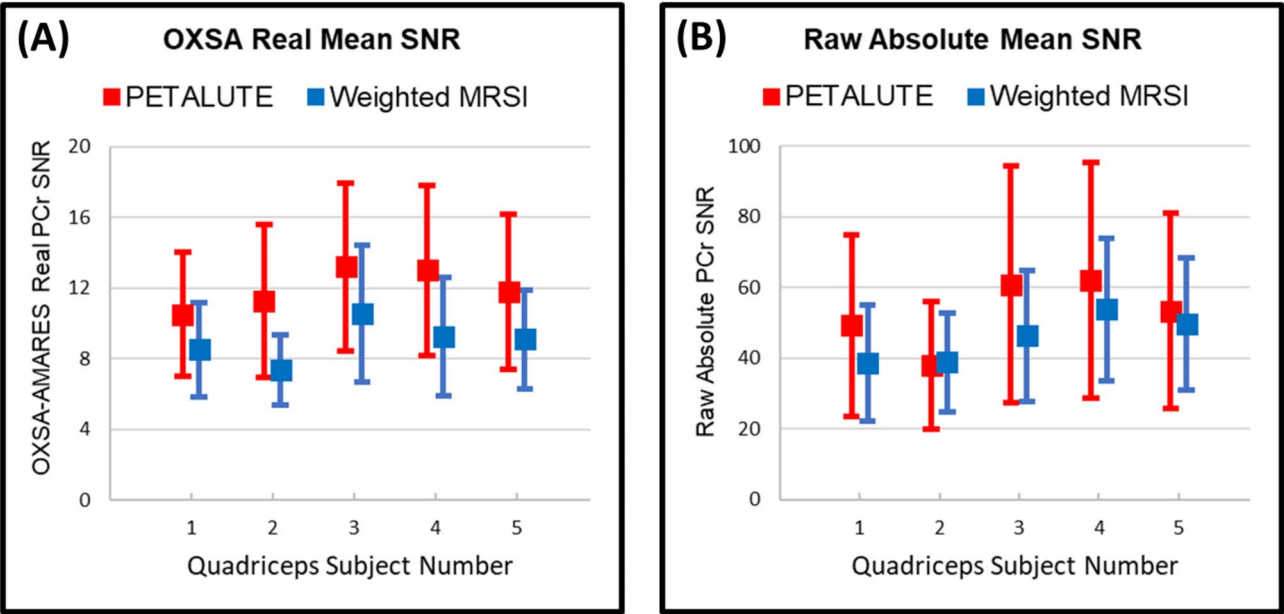


**Fig. 6.** (Left) Example axial slice raw PCr SNR maps from both acquisitions for one quadriceps subject. Both protocols clearly discriminate between high signal muscle tissue and low signal femur region. (Right) Unfiltered magnitude spectra from each method in the highlighted muscle (red) and bone (green) voxels scaled to the maximum PCr peak amplitude. Stated spectral SNR is for PCr peak.

## Discussion

### Experimental overview

This study demonstrates the feasibility of using PETALUTE <sup>31</sup>P-MRSI with a novel rosette k-space trajectory to acquire quality in vivo human subject data. Simulations showed the rosette trajectory produced acceptable image quality and SRF characteristics when compared to a conventional 3D weighted MRSI acquisition. Experimental phantom scans utilized a uniform Pi bottle solution, and the same scanning parameters were later applied to in vivo quadriceps subjects.



**Fig. 7.** (A) Measured PCr SNR (mean ± SD) from OXSA-AMARES quantifiable voxels across all five quadriceps subjects using each acquisition scheme and real data (Eq. 3). By this quantification metric, PETALUTE outperforms weighted MRSI by approximately 34% in vivo. (B) Measured raw PCr SNR (mean ± SD) from quantifiable voxels across all five quadriceps subjects and bottle phantom using each acquisition scheme and absolute data (Eq. 4). By this quantification metric, PETALUTE outperformed weighted MRSI by approximately 69% in phantom and 18% in vivo. Detailed results are provided in Tables 2 and 3.

|                         | PETALUTE       | Weighted MRSI  |
|-------------------------|----------------|----------------|
| Subject 1               | 10.50 (± 3.49) | 8.51 (± 2.66)  |
| Subject 2               | 11.26 (± 4.32) | 7.37 (± 1.97)  |
| Subject 3               | 13.21 (± 4.75) | 10.54 (± 3.88) |
| Subject 4               | 12.99 (± 4.83) | 9.24 (± 3.35)  |
| Subject 5               | 11.78 (± 4.42) | 9.11 (± 2.79)  |
| Total quantified voxels | 1070           | 947            |
| Mean CRLB               | 2.18%          | 2.56%          |
| Overall Leg PCr SNR     | 11.95 (± 4.39) | 8.95 (± 3.00)  |

**Table 2.** Mean in vivo PCr SNR (mean ± SD) from quantifiable voxels in individual subjects using OXSA-AMARES Eq. 3. With matched voxel size and acquisition resolution, PETALUTE outperforms weighted MRSI acquisition in measured SNR by 34% ( $p < 0.001$ ).

UTE advantages

The novel acquisition’s 70-μs acquisition delay is substantially lower than the 300-500-μs delays in previously published UTE <sup>31</sup>P-MRSI methods<sup>49,50</sup>, minimizing transverse signal decay and first-order dephasing. Accurate phasing is key to spectral fitting and quantification of real spectral data; when fitting parameters must be tailored to hundreds of voxels across a large volume, such as for high resolution 3D MRSI, the challenge of avoiding phasing errors is most apparent. As expected, all PETALUTE data were intrinsically devoid of noticeable first-order phasing, thereby streamlining the quantification process. The SNR gap between PETALUTE and weighted MRSI acquisitions was narrowed when solely considering absolute data (Eq. 4). This distinction might be partially explained by the absence of phase in these magnitude spectra, whereby the PETALUTE ( $T_E = 70 \mu s$ ) acquisition loses a portion of its advantage over conventional weighted MRSI ( $T_E = 2.3 \text{ ms}$ ). Notably, SDs for PETALUTE SNR were significantly higher (50% or more) compared to weighted MRSI. This elevated variation is partially explained by the novel acquisition’s significantly higher SNR; moreover, weighted MRSI’s slightly wider SRF engenders higher inter-voxel crosstalk, diminishing overall variation among quantified voxels.

Acceleration potential

Although these 36-minute acquisitions are quite lengthy, conventional ungated in vivo 3D <sup>31</sup>P-MRSI typically requires a minimum of 20 min at 3T. Compared to a weighted Cartesian trajectory, this novel rosette k-space

|                         | PETALUTE        | Weighted MRSI   |
|-------------------------|-----------------|-----------------|
| Subject 1               | 49.19 (± 25.72) | 38.50 (± 16.44) |
| Subject 2               | 37.96 (± 17.97) | 38.77 (± 14.02) |
| Subject 3               | 60.74 (± 33.49) | 46.31 (± 18.49) |
| Subject 4               | 61.96 (± 33.23) | 53.75 (± 20.08) |
| Subject 5               | 53.35 (± 27.57) | 49.62 (± 18.81) |
| Total quantified voxels | 1325            | 1378            |
| Overall Leg PCr SNR     | 52.83 (± 28.18) | 44.95 (± 17.70) |

**Table 3.** Mean in vivo PCr SNR (mean ± SD) from quantifiable voxels in individual subjects using raw Absolute Eq. 4. With matched voxel size and acquisition resolution, PETALUTE outperforms weighted MRSI acquisition in measured SNR by 18% ( $p < 0.001$ ).

|                                  | PETALUTE        | Weighted MRSI   | UTE/MRSI SNR ratio |
|----------------------------------|-----------------|-----------------|--------------------|
| OXSA-AMARES real in vivo PCr SNR | 11.95 (± 4.39)  | 8.95 (± 3.00)   | 1.34               |
| Raw absolute in vivo PCr SNR     | 52.83 (± 28.18) | 44.95 (± 17.70) | 1.18               |
| Raw absolute Phantom SNR         | 52.48 (± 34.6)  | 31.00 (± 9.84)  | 1.69               |

**Table 4.** Mean PCr SNR from quantifiable voxels across all five quadriceps subjects and bottle phantom using each method. With matched voxel size and acquisition resolution, PETALUTE consistently outperforms weighted MRSI acquisition in measured SNR ( $p < 0.001$ ).

pattern’s relative incoherence makes it a very suitable candidate for CS acceleration via undersampling. Applying undersampling factors of 2 to 4, as demonstrated previously in ultra-short transverse relaxation time ( $uT_2$ ) brain imaging<sup>26</sup> and sodium quantification<sup>30</sup>, could reduce PETALUTE  $^{31}\text{P}$ -MRSI’s  $T_A$  to 9–18 min (or less with fewer averages)<sup>57</sup>. Such ongoing investigations<sup>58</sup> could allow implementation of  $^{31}\text{P}$ -MRSI within realistic clinical constraints, while also being translatable to UHF research systems and higher resolutions.

As with all  $^{31}\text{P}$ -MRS, spectral quality can also see potential improvement via proton decoupling and nuclear Overhauser effect (NOE) enhancement, albeit with implications for SAR and measured metabolite ratios<sup>22</sup>. Furthermore, appropriately applied low-rank approximation and principal component analysis denoising have seen use in heightening SNR of MRSI data sets;<sup>59–61</sup> nevertheless, in the absence of ground truths or precise simulation, care must be taken in estimating metabolite concentration uncertainties after denoising.

Resolution and SBW

Many non-Cartesian acquisitions face restrictions in spatial resolution, SBW, and SNR due to available gradient hardware<sup>33</sup>. For example, spiral trajectories face reduced SNR while waiting to return to k-space center between spirals; this inefficiency is addressed by closed-loop, out-in trajectories<sup>62</sup>, but these remain impractical outside UHF animal gradient systems. Concentric rings can be similarly adjusted to meet needs with temporal interleaves<sup>43</sup>. Recent work with silent EPSI and gradient insert hardware shows remarkable promise in addressing these constraints<sup>63</sup>.

Clearly, SBW limitations are a significant challenge; although 2.0 kHz might be sufficient for  $^{31}\text{P}$ -MRS at 3T, such a SBW would only offer a spectral range of around 17 ppm at 7T. While this rosette acquisition sampled 48 points per petal every 480  $\mu\text{s}$ , the sequence remains highly customizable. By leveraging the second half of each petal (Fig. 1), it is possible to partially satisfy Nyquist criterion at even higher bandwidths and enable finer resolution reconstructions than the relatively coarse 8 mL voxels shown here. Additionally, this permits greater SBW acquisitions, opening the door to PETALUTE  $^{31}\text{P}$ -MRSI at UHF and  $^1\text{H}$ -MRSI at 7T and higher magnetic fields<sup>64</sup>. However, these petal halves are analogous to odd and even echoes of EPSI MRSI; since the timings between individual  $N_{pp}$  are not equidistant, such “full-petal” spectra will suffer from some degree of noise amplification and aliasing artifact.

Other limitations

Further experimentation is required in exploring the potential and limitations of PETALUTE MRSI. Notably, these scans focused on quadriceps muscle with plentiful PCr signal in a healthy volunteer population. However  $^{31}\text{P}$ -MRSI is frequently applied in measuring diverse brain, cardiac, and liver spectra, where nearby tissues may introduce contaminating metabolite signals. Minimal signal contamination was observed in noisy voxels within bony regions. Nonetheless, due to the relative uniformity of skeletal muscle spectra, it would be difficult to discern the rosette acquisition’s relatively incoherent aliasing. As clinical implementation of  $^{31}\text{P}$ -MRSI necessitates faster acquisition, future work will aim to assess accelerated performance in patient populations.

Notably, these acquisitions did not account for gradient delays in the reconstruction. Since rosette petals gradually evolve from  $K_z$  max (a straight line) to  $K_z = 0$  (a round circle), the slew rate and velocity change for petals in different  $K_z$  locations. Thus, the gradient delays will have variable impact, introducing an uncertainty in reconstruction which must be better accounted for in rigorous quantitative mapping. Similarly,  $B_1$ -homogeneity

can substantially impact measured metabolite signals. While operators performed manual transmit voltage calibration on the vendor adjustment platform before acquisition, variability in  $B_1$  remains a clear limitation. Future applications should incorporate  $T_1/B_1$  mapping to maximize quantitative accuracy across large volumes with multiple metabolites, especially at UHF.

## Conclusions

Using the quadriceps of five healthy volunteers at 3T, we investigated a potential application to  $^{31}\text{P}$ -MRSI using a novel 3D UTE rosette sequence. In comparison to conventional weighted Cartesian MRSI with matched bandwidth, nominal resolution, and acquisition time, the novel rosette acquisition provided competitive resolution and superior SNR with straightforward quantification. As this proof-of-concept study was limited to five subjects and a relatively homogeneous region of PCr-plentiful muscle, additional testing is required to demonstrate efficacy in differentiating diverse and diseased tissue regions.

## Data availability

Data are available upon reasonable request, by contacting the first author (bbozysk@purdue.edu).

Received: 5 April 2024; Accepted: 14 February 2025

Published online: 22 February 2025

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## Acknowledgements

This work was supported by grants to U.E. and S.S. from the Wellcome Trust Collaborative Award (223131/Z/21/Z). This project was funded with support from the Indiana Clinical and Translational Sciences Institute, funded in part by Award Number UM1TR004402 from the National Institutes of Health, National Center for Advancing Translational Sciences, Clinical and Translational Sciences Award.

## Author contributions

Conceptualization by U.E. & U.D.; Methodology contributions from all authors; Data collection by B.B., X.S. & U.E.; Data analysis by B.B., U.E., X.S. & W.T.C.; Results and conclusions reviewed and agreed upon by all authors. First manuscript draft and revision by B.B., U.E. & X.S.; Final revision and approval by all authors.

## Declarations

## Competing interests

The authors declare no competing interests.

### Additional information

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-90630-y>.

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