S1. Validation on phantom data

The method for time-resolved vCT generation was validated using an anthropomorphic digital phantom of the abdomen. The 4D XCAT phantom\textsuperscript{29} provided the CT data, whereas the 4D CoMBAT phantom\textsuperscript{28} allowed to simulate the MRI scan (with acquisition parameters as those used for patients’ data; paragraph 3.1) for vCT generation.

Materials and methods

The following dataset were used (Figure s1):

- Ground truth 4DCT with four phases (end-exhale, end-inhale, 30%-exhale, 30%-inhale);
- Reference 3D CT, which was obtained by applying a 6.00 mm shift in the superior direction to the end-exhale CT to simulate inter-fraction variations\textsuperscript{16};
- End-exhale MRI, corresponding to the end-exhale CT;
- Coronal/sagittal cine-MRI frame pairs corresponding to each respiratory phase of the 4DCT.

The reference vCT was generated from the reference CT and end-exhale MRI\textsuperscript{16} (paragraph 3.2.1). Then, the 3D DVFs were reconstructed\textsuperscript{27} (paragraph 3.2.3) and a vCT for each cine-MRI frame pair was obtained, corresponding to the 4DCT phases. A pseudo-clinical target was defined in the pancreas and warped on all the generated vCTs through the estimated DVFs. The 4DCT was used to optimize a treatment plan (Figure s2), whose dose was recomputed on all the available CT and vCT volumes.

The following metrics were evaluated:

- The geometrical error in the target, computed as the target center of mass (COM) distance between the vCT and the corresponding ground truth CT (COM error);
- The simulated inter-fraction variation\textsuperscript{16}, quantified as the target distance between the reference CT and the end-exhale CT (inter-fraction COM motion);
- The target motion, computed as the target COM distance between each CT and the end-exhale CT (4DCT COM motion);
- The dose error, calculated as the difference in terms of target $D_{5\%}$ (target $\Delta D_{5\%}$ error), $D_{95\%}$ (target $\Delta D_{95\%}$ error) and duodenum $D_{1\%}$ (duodenum $\Delta D_{1\%}$ error) between the dose distributions recomputed on the vCT and on the corresponding ground truth CT;
- Inter-fraction dose variations, obtained by comparing the dose recomputed on the reference CT with the planned dose on the end-exhale CT (target $\Delta D_{5\text{ inter}}$, target $\Delta D_{95\text{ inter}}$, duodenum $\Delta D_{1\text{ inter}}$);

- The motion impact on the dose distribution, calculated comparing the doses recomputed on the vCTs to the planned dose on the end-exhale CT (target $\Delta D_{5\text{ motion}}$, target $\Delta D_{95\text{ motion}}$, duodenum $\Delta D_{1\text{ motion}}$).

**Results**

The results are shown in Table s1. The geometrical error in the target is below 2 mm, i.e., the maximum CT voxel size (parameters in paragraph 3.1), and below the corresponding 4DCT motion. The dose error was $\leq 3.1\%$ for all the investigated metrics. The impact of motion on the dose distribution was more pronounced at the end-inhale respiratory phase, as expected for gated treatment plans.

**Conclusion**

In conclusion, the method presents proper geometrical and dosimetric accuracy. Its application to patients’ datasets is therefore feasible to estimate time-resolved (TR) vCTs from cine-MRI data.
**Figure s1.** Schematic for the validation of the method on a digital phantom.

**Figure s2.** Treatment plan with an anterior and two lateral beams. The contours represent: liver (yellow), pancreas (pink), GTV (red), pseudo-clinical CTV (orange), duodenum (light green), stomach (light blue).
Table s1. Phantom validation results for the reference vCT and the derived TR vCTs at the different respiratory phases.

| Volume | COM error [mm] | Inter-fraction COM motion [mm] | Target ΔD5 error | Target ΔD5 inter-fraction | Target ΔD95 error | Target ΔD95 inter-fraction | Duodenum ΔD1 error | Duodenum ΔD1 inter-fraction |
|--------|----------------|-------------------------------|------------------|--------------------------|-------------------|--------------------------|-------------------|---------------------------|
| Reference vCT | 1.07 | 6.00 | 0.0% | -0.2% | 0.0% | 0.0% | -25.2% | 0.5% | 12.8% |
| Phase | COM error [mm] | 4DCT COM motion [mm] | Target ΔD5 error | Target ΔD5 motion | Target ΔD95 error | Target ΔD95 motion | Duodenum ΔD1 error | Duodenum ΔD1 motion |
| End-exhale | 1.17 | 0.00 | 0.0% | 0.0% | 0.0% | 0.0% | 0.5% | 0.0% |
| 30%-exhale | 0.99 | 1.02 | 0.0% | -0.2% | -0.2% | 0.0% | 3.1% | 7.6% |
| 30%-inhale | 0.80 | 1.54 | -0.2% | 0.0% | -0.2% | -0.2% | 1.3% | 9.0% |
| End-inhale | 1.28 | 4.91 | -0.2% | 0.0% | 1.3% | -6.9% | -1.7% | 16.6% |
S2. Organs at risk dose

Table S2. Dose metrics to relevant organs at risk. The $D_{1\%}$ corresponding to the planned dose (“Plan”), to the recalculated dose on reference vCT (“Ref. vCT”) and on the 30%-exhale/30%-inhale vCTs (“30%-exhale/30%-inhale vCTs”) is listed. The median $D_{1\%}$ value is reported for the 30%-exhale/30%-inhale vCTs. The values in red are above the clinical constraint.

| Patient | Duodenum $D_{1\%}$ [Gy(RBE)] | Stomach $D_{1\%}$ [Gy(RBE)] |
|---------|--------------------------------|--------------------------------|
|         | Plan | Ref. vCT | 30%-exhale/30%-inhale vCTs | Plan | Rec. on ref. vCT | 30%-exhale/30%-inhale vCTs |
| P01     | 40.2 | 44.9     | 40.0                       | 26.4 | 23.0              | 23.9                        |
| P02     | 42.5 | 45.5     | 43.9                       | 26.9 | 27.4              | 27.1                        |
| P03     | 45.8 | 58.0     | 57.8                       | 5.3  | 1.6               | 2.0                         |
| P04     | 44.1 | 57.5     | 56.7                       | 35.8 | 35.3              | 35.2                        |
| P05     | 44.1 | 58.1     | 58.1                       | 43.3 | 57.8              | 57.5                        |
| P06     | 42.7 | 55.4     | 56.5                       | 33.2 | 44.9              | 51.5                        |
| P07     | 42.8 | 53.3     | 52.2                       | 39.5 | 38.5              | 38.9                        |
| P08     | 49.4 | 50.3     | 50.3                       | 1.9  | 1.3               | 1.6                         |
S3. Cycle-to-cycle variations

The respiratory surrogate (described in section 3.2.2) was used to identify relevant respiratory phases. The vCTs corresponding to the end-exhale phase were reconstructed to allow evaluating tumor position stability during gated irradiation, whereas the end-inhale respiratory phases were reconstructed to evaluate the variability of tumor motion amplitude.

The tumor position at end-exhale was stable and its variability was limited with respect to inter-fraction target displacement (Figure s3): the median (interquartile range) value of 3D motion was 1.02 (0.64) mm among all patients. The cycle-to-cycle variability of end-inhale motion is represented in Figure s4. In 3D, the difference between the estimated median displacement and the 4DCT motion amplitude was below 2.5 mm for all patient except P08 who presented an irregular breathing pattern (11.36 mm vs 4.00 mm in the TR vCT dataset and the 4DCT, respectively). Among all patients, the median breathing amplitude motion at end-inhale for vCTs was 4.15 mm, whereas it was 3.37 mm for the 4DCTs. A significant difference (Wilcoxon test, p=0.0078) was found between motion amplitude at end-inhale in the 4DCT and the 95th percentile of the motion amplitude in the TR vCT dataset.

Figure s3. Boxplots refer to target motion at reconstructed end-exhale vCTs with respect to the reference vCT, whereas blue stars indicate the inter-fraction target motion between the reference vCT and the pCT. The antero-posterior (A), right-left (B) and superior-inferior (C) components are shown for each patient.
Figure S4. Boxplots refer to target motion as estimated at end-inhale with respect to the reference, whereas blue stars indicate the end-exhale to end-inhale motion in the 4DCT. The antero-posterior (A), right-left (B) and superior-inferior (C) components are shown for each patient.