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Short Communication

Quality assurance process within the RAdiosurgery for VENtricular TAchycardia (RAVENTA) trial for the fusion of electroanatomical mapping and radiotherapy planning imaging data in cardiac radioablation

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ABSTRACT

A novel quality assurance process for electroanatomical mapping (EAM)-to-radiotherapy planning imaging (RTPI) target transport was assessed within the multi-center multi-platform framework of the RAdiosurgery for VENtricular TAchycardia (RAVENTA) trial. A stand-alone software (CARDIO-RT) was developed to enable platform independent registration of EAM and RTPI of the left ventricle (LV), based on pre-generated radiotherapy contours (RTC). LV-RTC were automatically segmented into the American-Heart-Association 17-segment-model and a manual 3D-3D method based on EAM 3D-geometry data and a semi-automated 2D-3D method based on EAM screenshot projections were developed. The quality of substrate transfer was evaluated in five clinical cases and the structural analyses showed substantial differences between manual target transfer and target transport using CARDIO-RT.

1. Introduction

Cardiac radioablation (RA) [1] of refractory ventricular tachycardia (VT) has been reported to reduce VT rates by 75 % [2–4]. Currently, no commercial product or clinically validated method for target transport from electrophysiology to radiation oncology treatment planning systems (TPS) are available. Several in-house solutions have been proposed [5–10], but most are based on specific data formats and platforms, while others are not publicly available. An alternative to direct target transfer is to apply a 17-segment decomposition of the left ventricle (LV) and overlay the decomposition onto the radiotherapy planning imaging (RTPI) [11,12]. The main disadvantage of this method is the lack of direct data registration and visualization in addition to possibly larger than necessary target volumes. The aim of this project was to develop and demonstrate the feasibility of an open, stand-alone, multi-platform solution for electroanatomical mapping (EAM)-RTPI registration and

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data display, dedicated specifically for quality assurance (QA) of the target transfer process from electrophysiological to radiation oncology systems for RA within the RAdiosurgery for VENtricular TAchycardia (RAVENTA) trial [16].

2. Materials and methods

The developed EAM-RTPI registration and data display software CARDIO-RT implements three data registration strategies: 17-segment, 3D-3D [7], and 2D-3D registration (Supplementary Table 1). CARDIO-RT is available free of charge upon request to the last author.

The 17-segment registration model (Supplementary Fig. 1) employs the "Image Processing Toolbox™", "Phased Array System Toolbox™", and "Statistics and Machine Learning Toolbox™" [12]. In CARDIO-RT, a 3D 17-segment model is generated after importing the manually delineated CT-based LV contours. To extract the 17 segments, CARDIO-RT implements a semi-manual method (Supplementary workflow for 17-segment registration). Regions of interest on the LV can be identified by listing one or more segment numbers. Since the computed tomography (CT) and the 17-segment model are matched, the location of abnormal tissue on the LV or the radiosurgical target region in CT coordinates can be obtained. The selected region(s) are displayed in a CT viewer wizard.

For 3D-3D registration, the "Image Processing Toolbox™" is employed. CARTO (Biosense Webster, Diamond Bar, CA, USA) and RHYTHMIA (Boston Scientific, Marlborough, MA, USA) EAM systems are supported. The mapping system is selected at the beginning, as the exported data formats vary (CARTO: one (.mesh file) or two files (.mesh file and _car.txt file); RHYTHMIA: MATLAB.m data format). The LV and aorta contour data are imported, followed by the EAM data. For contours, the aorta is shown in black and the LV in red. For the EAM data, the LV and part of the aorta are shown in blue, and the manually selected green points represent the target. A projection plane (cranial/left-lateral/posteroanterior) is selected. The EAM point cloud is moved stepwise by elementary planar transformations. When the registration is complete, the target is exported in DICOM-RT format. The CT data set and DICOM-RT file can be imported into the visualization sub-wizard to show the target in CT slices.

2D-3D registration employs the "Image Processing Toolbox™" and "Phased Array System Toolbox™". The target is delineated in the EAM (Fig. 1) and screenshots of this target in standardized anatomical viewing directions are saved. The CT-based LV contours and one or more EAM screenshots are imported into 2D-3D EAM-RTPI-registration. The user selects an anatomical viewing direction (active projection direction). The planar LV projection is overlaid onto the screenshot (active projection direction). A target curve is generated on the CT-based LV-contour by clicking on the appropriate intermediate points of the overlaid EAM screenshot that includes the previously delineated target. Anatomical landmarks can be selected for validation. Coordinates of the selected points can be recorded and added into the original contour file (DICOM-RT format). The CT data set can be imported into the wizard to visualize the target in CT slices. If necessary, coordinates of selected points can be exported in CSV format for further processing or visualization.

2.1. Participating centers and patient characteristics

CARDIO-RT was implemented and evaluated in five RA centers. Based on current consensus [13] and the RAVENTA trial protocol [16], RA treatment was considered in patients with VT where refractory to dose-escalated antiarrhythmic drug treatment and catheter ablation (CA) was infeasible or unsuccessful. Five VT cases, one from each center, were included. The study was approved by the local ethics commissions. In case 1, the 2D-3D registration tool was not finalized at the time of treatment and was applied in retrospect. For cases 3 and 4, structural analyses of the manually transferred targets with targets obtained from

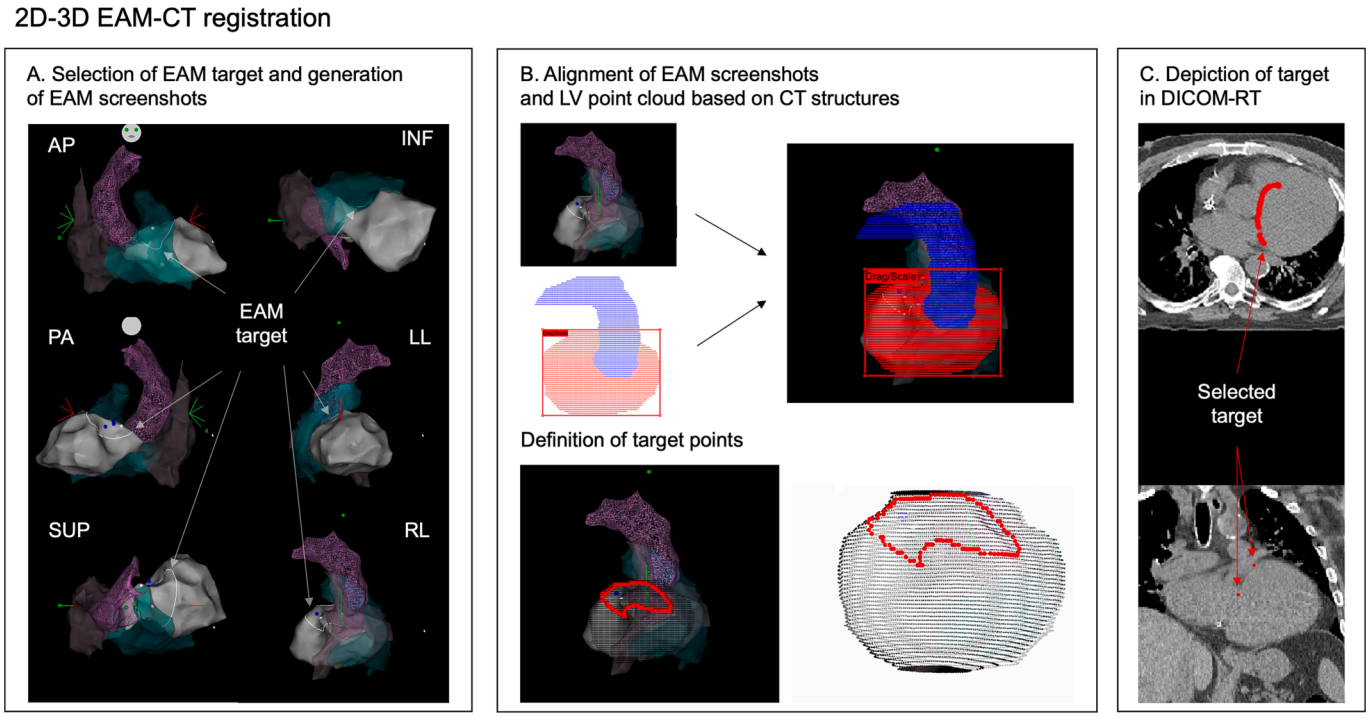

Fig. 1. The workflow of the 2D-3D EAM-RTPI registration. (A) Selection of the EAM target (white arrow) and generation of the EAM screenshots in different views from the invasive three-dimensional mapping system (right ventricle in green, left ventricle in grey, aorta in magenta, and right atrium in brown; (B) Alignment of the EAM screenshots and LV point cloud based on the CT structures and definition of the target points; (C) Depiction of the target in DICOM-RT. Abbreviations: AP = anteroposterior; CT = computed tomography; DICOM = Digital Imaging and Communications in Medicine; EAM = electroanatomical mapping; INF = inferior; LL = left lateral; LV = left ventricle; PA = posteroanterior; RL = right lateral; SUP = superior. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2D-3D registration were performed. In case 4, the EAMapReader [7] was employed. The fifth case examined a target transfer with a failed RA (Supplementary Table 3). The participating experts (electrophysiologists, radiation oncologists, and medical physicists) at each center were trained at the national workshop for cardiac RA in Germany and/or had previous experience in RA. Each center provided case data (epicrisis, 12-lead surface ECG, EAM and contrast-enhanced cardiac CT; Supplementary Table 2).

2.2. Target delineation for RA

EAMs of the cardiac chamber were obtained using CARTO, RHYTHMIA or EnSite (Abbott Laboratories, Chicago, IL, USA). Time-resolved thoracic treatment planning CT was performed for RTPI. ECG-gated contrast-enhanced cardiac CT was acquired in the diastolic phase. Target regions for RA were manually contoured on several EAM screenshots by electrophysiologists at each center (Fig. 1 & 2, Supplementary workflow for EAM-RTPI registration). The myocardial wall was delineated on the contrast-enhanced ECG-gated CT and registered with the planning CT. The target region was manually remodeled by interdisciplinary teams on the planning CT as a 3D structure [14] (Velocity and Eclipse v15 (Varian, Palo Alto, CA, USA), Monaco (Elekta, Stockholm, Sweden), and Precision (Accuray, Sunnyvale, CA, USA)). 2D-3D and 3D-3D matches were applied as a QA measure for the accuracy of the clinical target volume (CTV) transfer. If major modifications arose, the manually transferred CTV was revisited (cases 1–4). For case 5, the software was applied retrospectively on an EAM acquired after RA.

2.3. Structure analysis

CTVs were manually transferred from EAM to planning CT. Slice-by-slice CTV transfer by 2D-3D match to the CT was performed. CTV transfer by 3D-3D to the CT and transfer to the 17-segment model was conducted automatically. All 2D-3D, 3D-3D, and 17-segment matching were checked and/or performed by the study center. CTVs generated by manual transfer and using CARDIO-RT (2D-3D and 3D-3D) were compared for cases 3 and 4 and analyzed with Velocity (Version 3.2.1, Varian, Palo Alto, CA) [14].

3. Results

In case 1, EAM (Supplementary Fig. 2a) showed two possible target regions in the anteroseptal region of the LV and in proximity of an aneurysm of the LV in the basolateral region (for details see supplementary case histories and supplementary EAM-RTPI registrations). Based on the location of the previous CAs and the morphology of the VT, it was decided to only treat the left anteroseptal region. The mesh data, aorta contours from the CT delineation and LV before and after manual registration (moving the mesh data in three planar views until optimal alignment was reached) and software-based CTV could be transferred to the CT (Supplementary Fig. 2b-k). Based on 4D-CT, treatment was planned adapting the manually planned CTV with 3D-3D EAM-RTPI registration.

In case 2, data of cardiac MRI and contrast-enhanced CT in the systolic and diastolic phase were used for CTV verification and plausibility check due to scarring after myocarditis and several CAs (Supplementary Fig. 3a-c). The CT and MRI data suggested slightly different regions as possible targets. 2D-3D registration was performed based on EAM data and confirmed the results of the manual registration. Final CTV was obtained as a union of the target regions defined on CT and MRI.

In case 3, a large area of low voltage was recorded at the inferior/septal/basal/mid ventricular portion of the LV. Programmed ventricular stimulation with the ICD reproducibly induced a sustained monomorphic VT with an exit site in the inferior basal scar area corresponding to segment 4 (Supplementary Fig. 4). RA was performed by employing the manually transferred CTV adapted by 2D-3D and 3D-3D transfer. Comparison between manual, 2D-3D and 3D-3D registration showed high variation in CTV contours (Supplementary Table 4), with the smallest CTV observed for 3D-3D, followed by manual registration and 2D-3D. The surface area differed between registration methods, with the smallest surface area reported for 3D-3D, and the highest for the manual transfer. Axial, coronal and sagittal location of the center differed between registration methods. Using 2D-3D as reference, 3D-3D showed higher conformity than manual registration and a smaller Hausdorff distance.

In case 4, a large low voltage zone spanning the anterior/posterolateral/inferior/basal LV suggested an epicardial substrate with endocardial exits at these sites. The EAM target spanning the basal low voltage zone was transferred to the CT. A transmural ITV and planning target volume were planned taking into account respiratory motion (Monaco, Elekta AB; Supplementary Fig. 5). EAM-RTPI transfer was confirmed by 2D-3D. Comparison between manual and 2D-3D registration showed a conformity of 0.5 in CTV contours (Supplementary Table 4; Supplementary Fig. 6).

In case 5, target volume was defined by manual EAM-RTPI transfer. A comparison of the manually defined CTV with the target volume acquired from CARDIO-RT prior to RA was not possible, as the software was not available and a full EAM could not be obtained due to an LV apical thrombus. Despite RA, sustained VT recurred with recurrent conversion attempts. An additional invasive CA was performed three weeks after RA in segment 7, successfully terminating the VT. Retrospectively, CARDIO-RT registration was performed using the EAM data from the successful CA and the CTV from the previously performed RA. Accordance with the volume selected as RA target was observed (Supplementary Fig. 2). Retrospective analysis with CARDIO-RT revealed that RA was performed more apical to the region of the successful CA

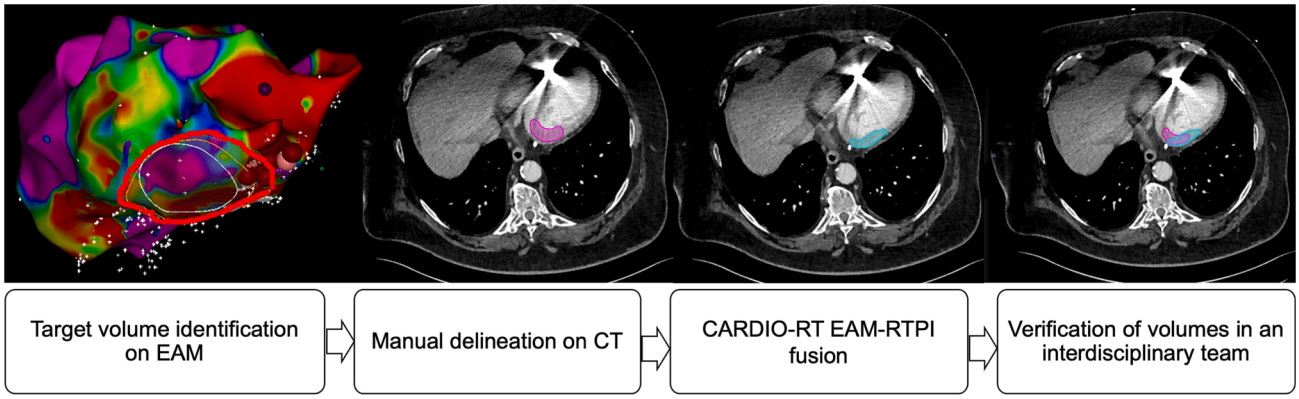

Fig. 2. Workflow of target identification, manual delineation, CARDIO-RT EAM-RTPI fusion and verification during the quality assurance process.

(Supplementary Figs. 7, 8).

4. Discussion

Feedback from the participating centers confirmed that CARDIO-RT is easy to use and requires minimal additional training. The same step sequence is used for any platform combinations (catheter-, CT-, radiation oncology systems). Target volumes and further anatomical structures can be easily visualized in 3D, with automatic labeling of the viewing directions. In comparison with previous methods that require the input of 3D mesh data [5,7,8,10], with the proprietary format of the mesh data being subject to changes without notice, the input requirements for 2D-3D registration (screenshots from standardized anatomical viewing directions) are minimal. Compared to 17-segment decomposition, CARDIO-RT allows for a more accurate data transfer as it shows the precise region chosen on the EAM data [15]. If new features are warranted, e.g. ECG data, these can be included in the MATLAB wizard [9].

The CARDIO-RT software was successfully employed as a QA measure in five patient cases within the multi-center multi-platform RAVENTA trial [16]. We observed the difference between manual transfer and two semi-automatic methods to be substantial, underlining the limited accuracy of manual target transfer, especially when considering that it was performed and approved by an interdisciplinary team with exceptional expertise in the field [14]. In case 4, the new 2D-3D registration method was compared to the previously published EAMap-Reader [7], showing high conformity of target volumes in both registration methods. Anatomical landmarks marked and integrated for both EAM data and CT-based LV contour data provided an additional tool for spatial validation of the registration result. In case 5, CARDIO-RT provided a retrospective verification based on newly acquired EAM data revealing why prior RA may not have been successful.

Due to limited data availability (cases 1&2: as the manually transferred CTV was not stored, structural CTV comparisons were not possible; case 5: EAM data prior to RA could not be included), a full validation of the CARDIO-RT software was not yet possible. Since RA for VT is a new procedure, patient numbers are limited and no larger scale clinical trial has been performed until today [2].

In conclusion, the new method for EAM-RTPI registration, 2D-3D registration, overcomes difficulties and limitations of earlier mesh data registration methods. 2D-3D registration was implemented in a freely available, stand-alone software system (CARIO-RT) and evaluated in a small series of patients. The new approach is suitable for any EAM-platform. The main visually intuitive registration step may reduce the risk of large transfer errors. Initially, the provided tools could be used to provide a second opinion on the validity of any manual or other method for target transfer.

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Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Boda-Heggemann reports consulting fees from EBAMed SA and a research grant from Elekta, outside the submitted work. Dr. Andratschke reports grants from SPHN Imaging – Swiss National Funds, from Clinical Research Priority Program University of Zurich, during the conduct of the study; personal fees from Debiopharm, personal fees from Astrazeneca, grants, personal fees and non-financial support from ViewRay, grants from Brainlab, outside the submitted work. Dr. Buergy reports consulting fees by NB Capital ApS / Nordic Biotech, honoraria by b.e. Imaging GmbH and participation on a Data Safety Monitoring Board or Advisory Board by PharmaMar S.A., outside the submitted work. Dr. Krug reports research funding by Merck KGaA, outside the submitted work. Dr. Saguner received educational grants through his institution from Abbott, Bayer Healthcare, Biosense Webster, Biotronik, Boston Scientific, BMS/Pfizer, and Medtronic; and speaker /advisory board fees from Abbott, Bayer Healthcare, Daiichi-Sankyo, Medtronic and Novartis, outside the submitted work. All other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2022.12.003.

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