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CARDIOVASCULAR IMAGES

# New Method CMR-Guided Endomyocardial Biopsy in Suspicion Context of Isolated Cardiac Sarcoidosis

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In 2020, a 34-year-old female patient presented with cardiac arrest due to ventricular fibrillation. Initial investigations concluded it to be a case of myocarditis. An ECG (EKG) revealed a right bundle branch block, elevation of troponin I levels (63 ng/L, n<32 ng/L), while an echocardiogram showed a normal left ventricular size and left ventricular ejection fraction at 60% with septal hypokinesia. Invasive coronary angiogram and a pharmacological test (methylergometrine) showed normal results. A subsequent cardiovascular magnetic resonance (CMR) study revealed a focal, nearly transmural area of late gadolinium enhancement (LGE) localized in the medial section of the septum without corresponding first-pass perfusion defect. The same area demonstrated a slightly elevated regional native T2 value of 54.2 ms on T2 mapping acquisition (GRE single-shot FLASH, MAGNETOM Skyra; Siemens; Figure 1; Videos S1 and S2). To confirm the inflammatory nature of the disease and rule out systemic sarcoidosis, a positron emission tomography (PET)/computed tomography (CT) with $^{18}$F-flurodeoxyglycose (FDG) was performed, which revealed uptake in the septal wall, exactly at the same position than that of the initial LGE image, with no extracardiac activity. As a result, the patient received a subcutaneous implantable cardioverter defibrillator.

Due to the uncommon pattern of the LGE image, a new evaluation was planned after 6 months to rule out cardiac sarcoidosis by new PET/CT-FDG. Nonetheless, a subsequent clinical assessment was not performed, and the patient remained without symptoms until 2022 when she encountered a new episode of arrhythmia that led to an appropriate shock by subcutaneous implantable cardioverter defibrillator. A radiofrequency endocavity ablation of the right ventricle was performed without the areas causing the arrhythmia been clearly identified. Subsequently, PET/CT-FDG was performed, which revealed exactly the same results as in the first PET/CT-FDG examination. A new CMR was not performed since the patient was implanted with a subcutaneous implantable cardioverter defibrillator. The position of subcutaneous implantable cardioverter defibrillator was likely to generate significant metal artifacts. In addition, PET/CT-FDG showed uptake in the septal wall once again exactly at the same position than that initially identified on the LGE image; so we decided to use the information from the first CMR.

To address this rhythmic instability and to diagnose isolated cardiac sarcoidosis, an endomyocardial biopsy (EMB) was necessary in the small abnormal area identified by the LGE and PET/CT images (Figure 1). To improve the accuracy of EMB, a novel 3-dimensional imaging process, magnetic resonance imaging–guided EMB was used. More precisely, this method uses deep learning to segment 3-dimensional images and to build a myocardial model with fibrosis information based on the LGE image. The LGE image (fibrosis tissue) is currently manually segmented (Figure 2). These methods have been implemented on the free and open-source software CamitTK (https://camitk.imag.fr). This model can be displayed on the same screen and using the same view than the per-operative fluoroscopic images, allowing to improve EMB precision. These additional pieces of information were used to choose right ventricular EMB, and the procedure was performed using guidance from





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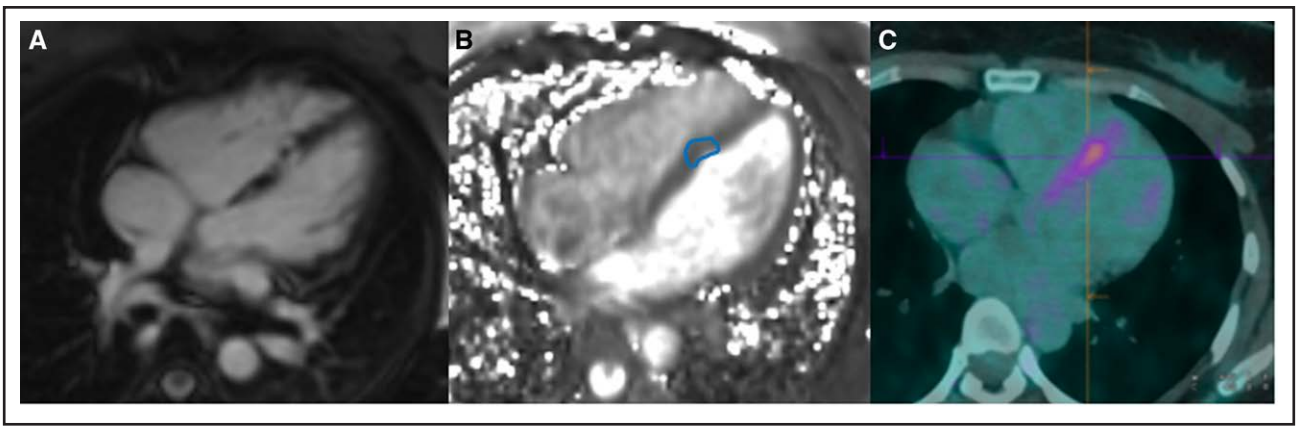


**Figure 1. Multimodal imaging analysis.**
Cardiac magnetic resonance horizontal long-axis view showed abnormal single focal abnormality late gadolinium enhancement image in the medial part of the septum (**A**) in accordance of slightly elevated regional native T2 value (blue region of interest [ROI]; **B**) and of uptake in the septal wall by positron emission tomography/computed tomography with $^{18}$F-flurodeoxyglycose (**C**).

the preoperative planning model. Left ventriculography in 30° RAO (Video S3) and 30° LAO (Video S4) was performed, and the preoperative planning model was oriented according to a similar view to correctly locate the target (Figure 3). EMB was successful (Video S5), and anatomopathological analysis showed no inflammatory elements in favor of chronic myocarditis and noncaseating granulomas in favor of sarcoidosis confirmed by immunohistology (CD3+ T cells and CD68+ macrophages) and no viral genome detection/replication by viral polymerase chain reaction but a cross-linked fibrosis and irregular cardiomyocytes with some degree of anisokaryosis (Figure S1). Finally, desmosomal gene-related arrhythmogenic left ventricular cardiomyopathy was pointed out.

There is a strong overlap between myocarditis, desmosomal gene-related arrhythmogenic cardiomyopathy, and isolated cardiac sarcoidosis.[1] However, the management of these conditions is different, and it is important to perform an appropriate diagnosis. Despite imaging progress, it is difficult to differentiate disease, and in patients having no extracardiac disease upon whole-body FDG-PET,



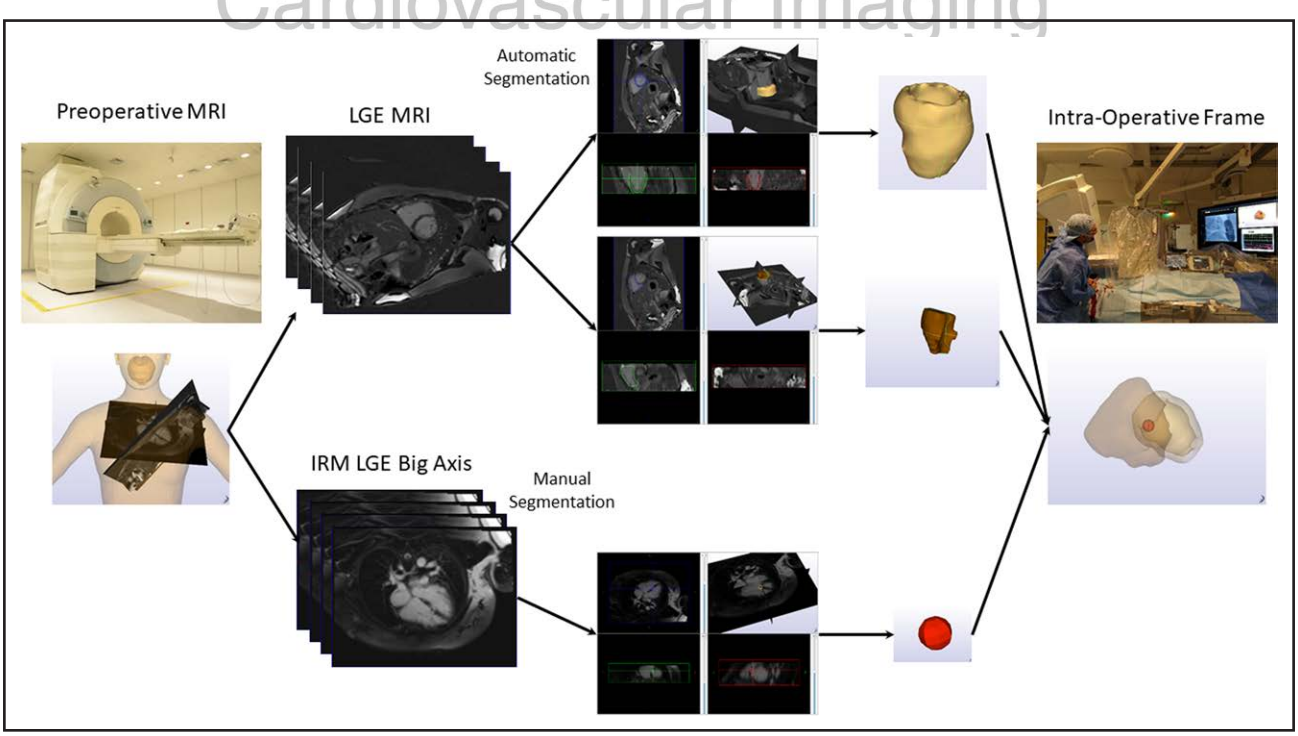


**Figure 2. New method cardiac magnetic resonance–guided endomyocardial biopsy.**
New method based on deep learning has been developed to build a myocardial model with fibrosis information based on late gadolinium enhancement (LGE) image. IRM indicates imaging of resonance magnetic; MRI, magnetic resonance imaging.

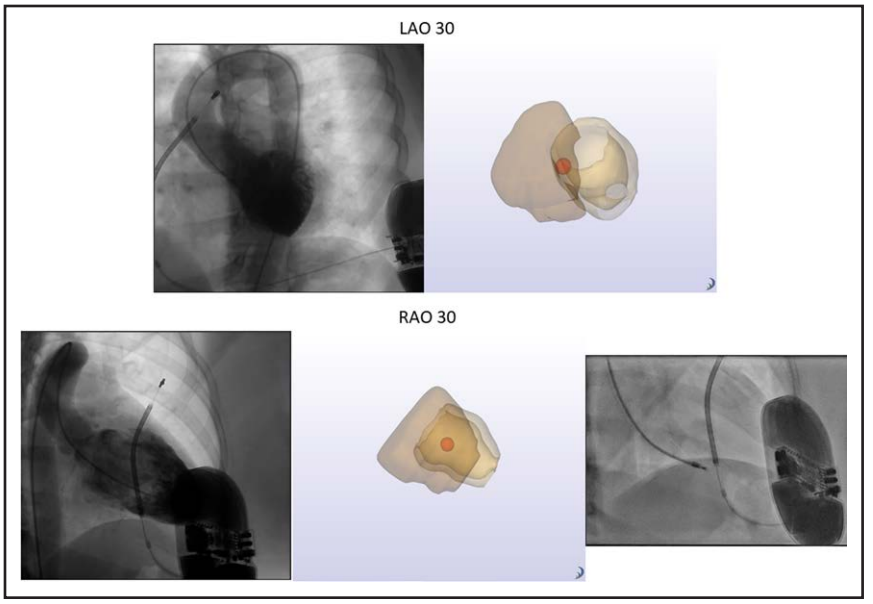


**Figure 3. Comparison between ventriculography and myocardial model.**
Preoperative planning model oriented in 30° right anterior oblique (RAO) and in 30° left anterior oblique (LAO).

EMB is necessary to confirm cardiac sarcoidosis.[2] However, EMB has low sensitivity (30%) due to its focal nature.[3] Here, we propose a computer assistance system to clinically implement EMB. This system consists in a preoperative planning model generated by a new deep learning model providing spatial information. By creating a patient-specific numerical model of the heart, clinicians are provided with valuable assistance and guidance during the planning phase for optimal location and path selection for EMB procedures. This numerical model ensures safety and efficiency during the execution of the procedure. This application becomes especially crucial in cases where suspected isolated cardiac sarcoidosis is involved. Currently, the deep learning model only operates on CMR images. Ongoing advancements are underway to establish an automated myocardial fibrosis segmentation system within LGE images, aligning it with data derived from PET/CT-FDG, with special emphasis on the integration of 3-dimensional CT information. Our deep learning model uses CMR images, but the recalibration of 3-dimensional information obtained from different imaging techniques could enable its development for use with PET/CT or PET/CMR and thus help other entities requiring guided EMB.

The preoperative planning model offers essential spatial information, facilitating the integration of multimodal data. By leveraging this information, clinicians can make informed decisions on the best sites for EMB, whether it be in the left or right ventricular regions, specifically targeting abnormal areas previously identified through CMR and PET/CT imaging. This approach enhances the accuracy and efficacy of the procedure, enabling better targeting of the affected tissue and improving overall patient outcomes. Finally, we have presented a novel method for CMR-guided EMB, specifically designed for cases where isolated cardiac sarcoidosis is suspected. The key aspect of this method is its automation, which aims to develop user-friendly software easily accessible to clinicians in the catheterization laboratory. By automating CMR-guided EMB, we expect to achieve enhanced efficiency, accuracy, and diagnostic capabilities, empowering clinicians to make well-informed and timely decisions in managing patients with suspected cardiac sarcoidosis.



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### Disclosures

None.

### Supplemental Material

Figure S1
Videos S1–S5

## REFERENCES

1. Corrado D, van Tintelen PJ, McKenna WJ, Hauer RNW, Anastastakis A, Asimaki A, Basso C, Bauce B, Brunckhorst C, Bucciarelli-Ducci C, et al; International Experts. Arrhythmogenic right ventricular cardiomyopathy: evaluation of the current diagnostic criteria and differential diagnosis. *Eur Heart J.* 2020;41:1414–1429. doi: 10.1093/eurheartj/ehz669
2. Trivieri MG, Spagnolo P, Birnie D, Liu P, Drake W, Kovacic JC, Baughman R, Fayad ZA, Judson MA. Challenges in cardiac and pulmonary sarcoidosis: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020;76:1878–1901. doi: 10.1016/j.jacc.2020.08.042
3. Birnie DH, Kandolin R, Nery PB, Kupari M. Cardiac manifestations of sarcoidosis: diagnosis and management. *Eur Heart J.* 2017;38:2663–2670. doi: 10.1093/eurheartj/ehw328