Septal scar predicts failure of lead advancement to the left bundle area

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Abstract

Background Left bundle area pacing is growing in use both for bradycardia pacing and cardiac resynchronization, but implants are not always successful. We prospectively studied consecutive patients to determine whether septal scar contributes to implant failure. Methods Patients scheduled for left bundle area pacing, using the 3830 Selectsecure lead were prospectively enrolled. All patients underwent standardized scar assessment by cardiac MRI with late gadolinium enhancement imaging. Scar burden was quantified as the proportion of basal septal segments showing late enhancement. Results 35 patients were recruited: 29 male, mean age 68 years, 10 with ischemic and 16 with dilated cardiomyopathy. Pacing indication was bradycardia in 26% and cardiac resynchronization in 74%. In 5/35 (14%) it was not possible to advance the lead through the ventricular septum. Basal septal late gadolinium enhancement was significantly more extensive in these patients (median 67%, IQR 58-69.5) compared to the other 30 (median 10%, IQR 0-20, p = 0.0006). There was no significant correlation between the paced QRS duration achieved and the extent of basal septal scar (r = 0.06, P = 0.75). Conclusions Failure to deliver a lead to the left bundle area is strongly associated with a (very) high burden of scar in the basal septum. Once the lead is delivered, however, the electrical response is independent of scar burden. This suggests that it would be worth developing delivery tools to tackle scarred basal septa, because if the lead could be delivered the electrical capture might still achieve a narrow QRS.

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Methods

Patients scheduled for left bundle area pacing, using the 3830 Selectsecure lead were prospectively enrolled. All patients underwent standardized scar assessment by cardiac MRI with late gadolinium enhancement imaging. Scar burden was quantified as the proportion of basal septal segments showing late enhancement.

Results

35 patients were recruited: 29 male, mean age 68 years, 10 with ischemic and 16 with dilated cardiomyopathy. Pacing indication was bradycardia in 26% and cardiac resynchronization in 74%.

In 5/35 (14%) it was not possible to advance the lead through the ventricular septum. Basal septal late gadolinium enhancement was significantly more extensive in these patients (median 67%, IQR 58-69.5) compared to the other 30 (median 10%, IQR 0-20, p = 0.0006).

There was no significant correlation between the paced QRS duration achieved and the extent of basal septal scar (r = 0.06, P = 0.75).

Conclusions

Failure to deliver a lead to the left bundle area is strongly associated with a (very) high burden of scar in the basal septum. Once the lead is delivered, however, the electrical response is independent of scar burden. This suggests that it would be worth developing delivery tools to tackle scarred basal septa, because if the lead could be delivered the electrical capture might still achieve a narrow QRS.

Key words

CRT Cardiac resynchronization therapy

LBP Left bundle area pacing

BVP Biventricular pacing

LGE Late gadolinium enhancement

RWPT R Wave peak time

Introduction

Left bundle area pacing (LBP) promises a revolution for treating bradycardia and achieving cardiac resynchronization[1–4], but has lower success rates in ischemic cardiomyopathy[2,3,5]The reasons are not clear but may include difficulty in reaching the left bundle area or stimulating it adequately. For such patients, operators therefore sometimes aim for His bundle pacing accepting the potential for higher capture thresholds and lower amplitude R waves.

The technique for LBP involves deploying the lead through the interventricular septum, which may be scarred in patients in patients with ischemic cardiomyopathy. Late gadolinium enhancement (LGE) on MRI is a reliable way of detecting, localizing and quantifying myocardial scar[6,7]non-invasively. However, the 3830 SelectSecure lead (Medtronic, Minneapolis, MN) when implanted for LBP is currently not MRI conditional, and therefore post-procedure scanning would be more challenging.

We therefore conducted a systematic protocol of MRI scanning before attempting LBP, to test whether localized late gadolinium enhancement might reveal the mechanism of the difficulties seen in some patients.

Methods

Study population

This was a prospective, single center observational study. Consecutive patients referred to one electrophysiology team, between October 2019 to August 2021, for device implantation for bradycardia or cardiac resynchronization were offered conduction system pacing which was explained to them as a newer non-standard method which may have advantages but was associated with a research MRI scan. The study was approved by the local ethics committee (REC 19/YH/0174). Consenting patients were enrolled. They underwent a pre-implant cardiac MRI to which the cardiac catheterization laboratory team were kept blinded.

Cardiac MRI

Cardiovascular magnetic resonance was performed in a 1.5 Tesla (Aera, Siemens Medical Solutions, Erlangen, Germany) using a standard clinical scan protocol including LGE imaging following a bolus of 0.1mmol/kg of Gadobutrol (marketed as Gadovist, Bayer Pharma AG, Berlin, Germany). In the majority of cases, scar imaging was undertaken using a free-breathing motion corrected sequence as detailed by Captur *et al*[8]. (25/35, 71%) also had dark blood late gadolinium enhancement imaging which increases sensitivity for detecting subendocardial scar[9].

Image Analysis

Cardiovascular magnetic resonance imaging analysis was performed using CVI42 software (Version 5.13.7, Calgary, Canada) blinded to clinical parameters. The presence and extent of myocardial scar in the basal septum (defined as the inferoseptal and anteroseptal segments in the most basal 3 complete slices) was assessed by an experience level 3 CMR operator. The observer was aware of the hypothesis regarding the basal septum but had no access to information on the procedural outcome. Scar burden was quantified either using full width half maximum semiautomated technique[7]with manual review, or manually (for dark blood images). In the patients who had both images, the greater of the two scar quantifications was used. Scar extent was quantified as the percentage of the amount of myocardium in those segments.

Left bundle area pacing

LBP was carried out in the electrophysiology laboratory (Hammersmith Hospital, UK) electrocardiograms were recorded using the electrophysiology system (Boston Scientific, Natick, Massachusetts).

The C315His fixed curve sheath (Medtronic, Minneapolis, MN) was used to position the SelectSecure 3830 lead (Medtronic, Minneapolis, MN) onto the bundle of His. We mapped the His bundle and stored fluoroscopic image in the right anterior oblique view, and this was used as a roadmap. The lead was then advanced to basal right ventricular septum about 2cm below the His bundle. From that position it was deployed deep into the ventricular septum (Figure 1). A single operator (ZW) assessed the deliverability of the left bundle lead and the electrical response while blinded to the results of the cardiac MRI.

During lead advancement, we monitored impedance and time to peak R wave (RWPT) (time from the stimulus to peak R wave in lead V5 or V6) with unipolar pacing. Left bundle capture was confirmed by a right bundle branch block morphology with a terminal R wave in lead V1 and any of: 1- RWPT time $<$ 90ms, 2-The presence of left bundle branch potential (15-30ms before the QRS onset), 3-Transistion from non-selective to selective left bundle capture (Figure 2) or non-selective left bundle capture to myocardial only capture with change in pacing output or with programmed stimulation.[10]

Lead depth was assessed by placing the end of the sheath onto the septum and measuring the distance to the tip of the lead or by contrast injection. Furthermore, in cases where the lead was not advanced or left bundle was not captured, electrocardiographic monitoring showed left bundle branch morphology and the RWPT in V5/V6 remained $>$ 80ms.

We defined two modes of failure. Unsuccessful lead delivery was inability to advance the lead deep enough into the septum to reach the left bundle area. Unsuccessful left bundle capture was failure to stimulate the left bundle despite successful lead delivery.

Paced QRS duration during LBAP was used to assess electrical response. The QRS was optimized by allowing fusion with intrinsic right bundle conduction if possible.

Statistical analysis

Continuous variables were expressed as mean and standard deviation if normally distributed and mean (IQR) otherwise. Correlation were assessed by the Spearman rank correlation coefficient. Comparisons between groups were performed using the Mann Whitney U test. A p value $<$0.05 was considered statistically significant. Statistical analysis was conducted in RStudio using the tidyverse package.

Results

Patients

35 patients were enrolled (Table 1) in the study. Over two thirds had a CRT indication and one third had ischemic cardiomyopathy. Left bundle area pacing was achieved in 30/35 (86%) of patients.

Septal scar quantification

Late gadolinium enhancement was present in the basal septum in 26 of the 35 patients. There was considerable variation in extent, between 1% and 74% (Figure 3). Figure 3 shows a representative basal short axis slice in all 35 patients.

25 patients had both bright blood and dark blood images. In 9 patients (of whom 7 had ischemic cardiomyopathy), the dark blood revealed more scar. In 1 patient with amyloid the bright blood revealed more scar. In the rest bright blood and dark blood scar extent was equivalent.

Lead advancement, capture, and achievement of narrow QRS

Advancement to the left side of the septum was achieved in 30/35 patients (86%). Amongst those, left bundle capture was achieved in 30/30 (100%) patients.

In the 5 patients where lead advancement was not achieved, device indication was CRT in 5/5 (100%). In this group, 3/5 (60%) had ischaemic cardiomyopathy, 1/5 (20%) had dual pathology and 1/5 (20%) had amyloid. All 5 patients went on to have successful biventricular pacing devices.

In the 30 patients where lead advancement was achieved, device indication was CRT in 21/30 (70%) and bradycardia pacing in 9/30 (30%). In this group, 7/30 (23%) had ischaemic cardiomyopathy, 15/30 (50%) had non-ischaemic cardiomyopathy and 2/30 (7%) had dual pathology.

Narrow QRS (<130ms) was achieved in 28 of the 30 (93%) patients in whom the left bundle was captured. It was not achieved in two patients. In one, with left bundle branch block and extensive ischemic scar (39% of total myocardium), the QRS remained 140ms despite left bundle capture. In the other, with right bundle branch block and a very broad intrinsic QRS (206ms), the QRS did shorten substantially but only to 150ms.

Basal septal scar and success of lead advancement

There was significantly more basal septal scar in the patients where lead advancement failed (median 67% of myocardium, IQR 58 to 69.5) than patients where lead advancement was successful (median 10% of myocardium, IQR 0 to 20, p = 0.0006, Figure 4).

Basal septal scar and electrical response

The paced QRS duration showed no significant relationship (Figure 5) with the extent of scar in the basal septum (r = .06, 95% CI: -0.3-0.4, p = 0.75) and only a non-significant trend with scar in the whole left ventricle (r = 0.3, 95% CI:-0.06-0.6, p = 0.1).

Predicting advance ability of the lead from extent of basal septal scar

We constructed an exploratory analysis of the likelihood of delivering a lead, predicted from the extent of basal septal scar.

Discussion

This study finds that in patients with less than about 40% basal septal scar, the LBP lead (3830 SelectSecure) was always successfully advanced; in those with more than 60% basal septal scar, it was never successfully advanced. Importantly, once the lead is successfully advanced, the amount of basal septal scar has no impact on the QRS duration achieved. Finally, we observed that dark blood imaging is better able to identify ischemic scar and,

in agreement with previous research[9]is advisable in research or clinical practice where scar quantification is important.

Septal scar and failure to advance pacing lead to left bundle area

In this study, lead delivery was unsuccessful in 14% of patients. Our patient group was drawn from a tertiary center where advanced cardiomyopathy was over-represented. 82% had a form of cardiomyopathy and 34% had ischemic cardiomyopathy. Our center is often referred patients with severe disease. For example 88% of our non-ischemic cardiomyopathy patients had scar, which is a higher rate than other published cohorts[11], but may be due to selection bias in those being referred on for devices.

Early reports of left bundle area pacing were largely bradycardia pacing in patients with structurally normal hearts. However, extending its application to heart failure including ischemic cardiomyopathy inevitably brought higher failure rates[3].

Some authors have discouraged left bundle area pacing in ischemic cardiomyopathy for this reason[12,13], suspecting that scar in the basal septum might be to blame.

Our high-quality tissue characterization by MRI showed that even when there was scar, in 80% of cases the left bundle could be paced. What mattered was the extent of scar in the basal septum. There was a clear association between extent of scar and failure of lead advancement. Nevertheless, even at 50% basal septal scar, our data suggests that 70% of cases have successful lead delivery.

Moreover, in this study we used only the (SelectSecure 3830,Medtronic, Minneapolis, MN). It is possible that stylet driven leads or alternative tools may help overcome the problem of lead advancement in patients with extensive septal scar. As has occurred with other pacing modalities, development of more specific leads and delivery equipment is likely to improve success rates in the more challenging cases with extensive scar.

Implications of dual blood supply to the conduction system

Unlike myocardial tissue which generally has a single blood supply, much of the conduction system is supplied by more than one coronary vessel. This may explain why even when there is infarction severe enough to lead to substantial myocardial scarring, the electrical system in the basal septum can still be captured and achieve narrow complex activation of the ventricle.

In the patients where we failed to advance the lead due to the severity of basal septal scarring, we cannot test whether left bundle capture is possible or achieves a desirable QRS pattern. We should not assume that the answer is no, because within the patients where the lead could be advanced there was no significant sign of greater basal septal scar being associated with a worse electrical response. It is known that in biventricular pacing non-viability of the entire septum is associated with non-response[14]. but this does not necessarily mean that the conduction system cannot be captured at the septum to activate the rest of the ventricle.

Extensive myocardial scar might also cause uncoupling of the myocardium from the conduction system, which could give an activation pattern matching criteria for left bundle branch block, even when the proximal conduction system is functioning normally. This may be the explanation for the finding by Upadhyay et al that 36% of patients with left bundle branch block had intact conduction in the His-Purkinje fibers[15].

Utility of dark blood late gadolinium sequences

Accurate detection and quantification of the scar extent was a key part of this study. In addition to bright blood, we used dark blood late gadolinium enhancemnt. Dark blood sequences allow better delineation of subendocardial scar so is particularly useful in patients with ischaemic cardiomyopathy[9].

In 7 patients (five of whom had ischaemic scar in the septum), the full extent of scar was not appreciated on standrad bright blood sequences. It was only when dark blood late gadolinium enhancement sequences were utilised that the full extent of scar was appreciated. The key advantage is better appreciation of the border between the subendocardium and blood.

The findings from our study suggest that dark blood sequences should be carefully reviewed in patients who are due to undergo left bundle area pacing. This will ensure that patients with extensive fibrosis are reliably identified, which is likley to help with procedural planning.

Clinical implications

This study indicates that Cardiac MRI provides useful information before attempting left bundle pacing. Operators planning left bundle pacing should consider the presence and extent of basal septal scar in their procedural planning: if there is $< 50\%$ extent, lead advancement is very likely to be successful; if there is $>70\%$, lead advancement is very likely to fail. This can help the operator decide whether to try left bundle pacing and how persistent to be in the attempt.

Our research also suggests that patients would benefit from the development of better tools to penetrate an extensively scarred basal septum, because once the left bundle area is reached the scar extent may not impair successful stimulation. The mechanism of preserved simulation despite extensive scar may be the dual blood supply.

Study limitations

This was a single center study with only 35 patients. We cannot exclude the possibility that there is a small fraction of patients whom the lead can be advanced successfully but the left bundle cannot be captured.

LBAP is a relatively new procedure, and success may be limited by operator experience. In our cohort, the procedures were all performed by a single experienced operator. The patients where lead advancement was not achieved were widely distributed in terms of procedure dates, so it was not due to problems earlier on in the learning curve. The time-order of cases where lead advancement was not achieved was 5,7,11,29 and 36.

The distribution of our patient cohort is tilted toward a greater extent of scar because it is from a tertiary center with many cases of advanced heart failure. However, this does not detract from the observation that when basal septal scar was extensive, the lead was much less likely to be advanceable but (once advanced) the left bundle could be successfully stimulated.

Our center used only one type of lead for the left bundle. We cannot exclude the possibility that a different type of lead such as a stylet driven lead may have different advance-ability characteristics. Nevertheless, there is a clear need for better custom-made tools for this task.

Conclusions

Very high scar burden in the basal septum as assessed using cardiac MRI is a strong predictor of failure to deliver the lead to the left bundle area. However, once the lead is delivered, scar burden is no impediment to successful stimulation. Cardiac MRI is a useful pre-procedural planning step, and future development of specialised tools to advance a lead through a heavily scarred basal septum could be beneficial because it would likely still achieve a narrow QRS.

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Tables 1-2

Table 1. Demographics. Continuous variables are expressed as mean ± standard deviation

and discrete variables as numbers and percentages.

	All patients N = 35
Male	29 (83%)
Age (year)	68 ± 10
Device indication	
Bradycardia	9 (26%)
CRT	26 (74%)
Left ventricular ejection fraction (%)	Left ventricular ejection fraction (%)
All patients	45 ± 19
Bradycardia group	62 ± 11
CRT group	29 ± 8
Cardiomyopathy	29 (82%)
Ischaemic	10
Non-ischaemic	16
Dual pathology	3
Left ventricular dimensions	Left ventricular dimensions
LVED volume/ mL*	95 ± 25
Myocardial mass/g*	78 ± 24
Basal septum/mm	9 ± 1
ECG	
QRS duration	152 ± 23
QRS morphology	
LBBB	19 (53%)
RBBB	7 (20%)
IVCD	7 (20%)
Normal	2 (7%)

CRT cardiac resynchronisation therapy, IVCD intraventricular conduction delay, LBBB left bundle branch block, LVED left ventricular end-diastolic volume, RBBB right bundle branch block.* Figures corrected to body surface area.

Table 2 Post hoc model of the probability of lead delivery predicted from the basal septal scar burden expressed as a percentage of total basal septal myocardium.

Extent of Basal septal scar (%)	Probability of lead delivery
10	100%
20	100%
30	99%
40	95%
50	70%
60	24%
70	4%
80	1%
90	0
100	0

Figures 1-5 and central illustration

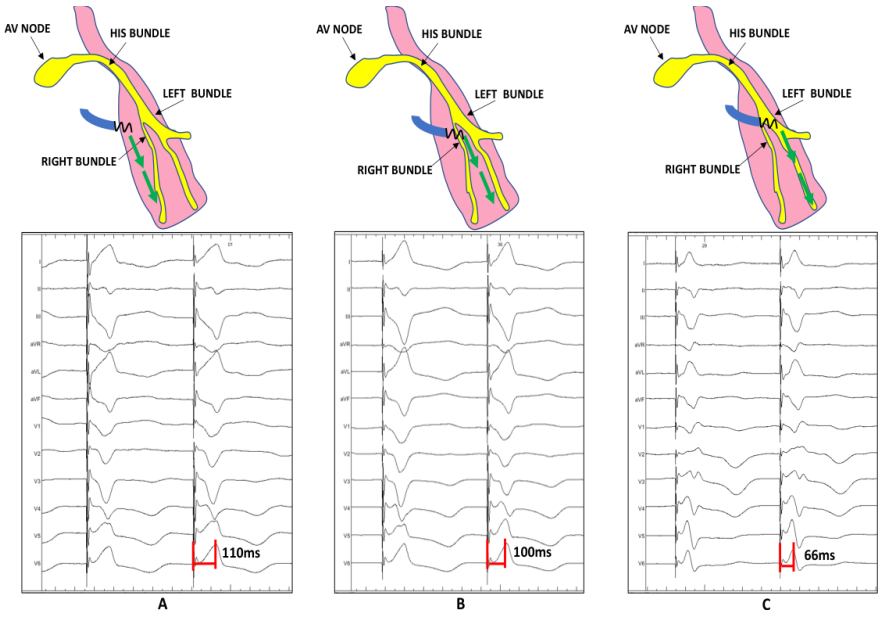

Figure 1. Left bundle area pacing by the transseptal technique, the green arrows the direction of electrical activation. **A** Left bundle lead at the right ventricular septum showing right ventricular septal capture. The ECG shows notched QRS in V1 and RWPT measures 110ms.**B** Left bundle lead in the mid-septum. The notch in lead V1 has progressed and RWPT has reduced to 100ms. **C** left bundle capture right bundle branch block in lead V1 with a terminal R wave (R prime) and RWPT 66ms.

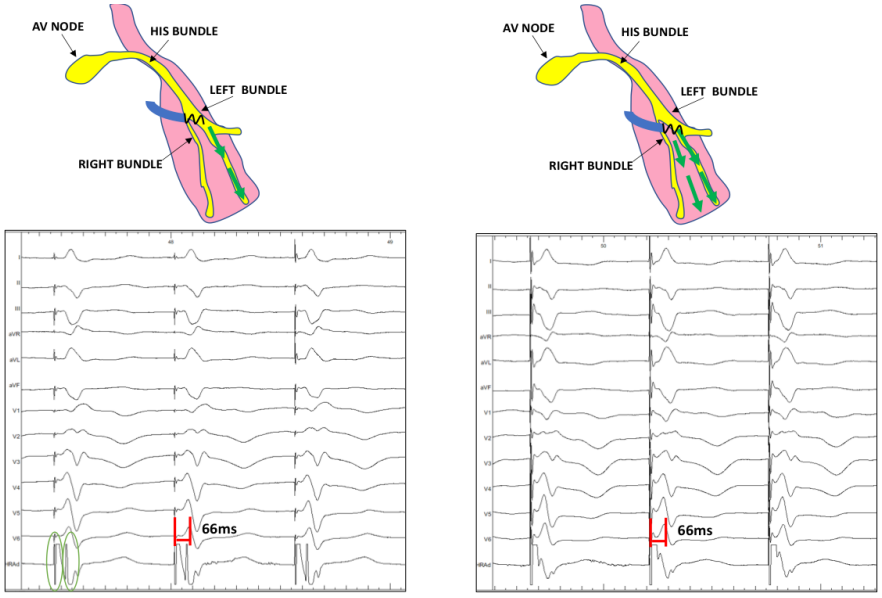

Figure 2. Selective and non-selective left bundle capture. The green arrows the direction of electrical activation. Left figure shows selective left bundle capture with an isoelectric line between the pacing spike and start of the QRS, EGM shows myocardial activation distinct from pacing stimulus (green ovals). Right non-selective left bundle capture with no iso-electric line.

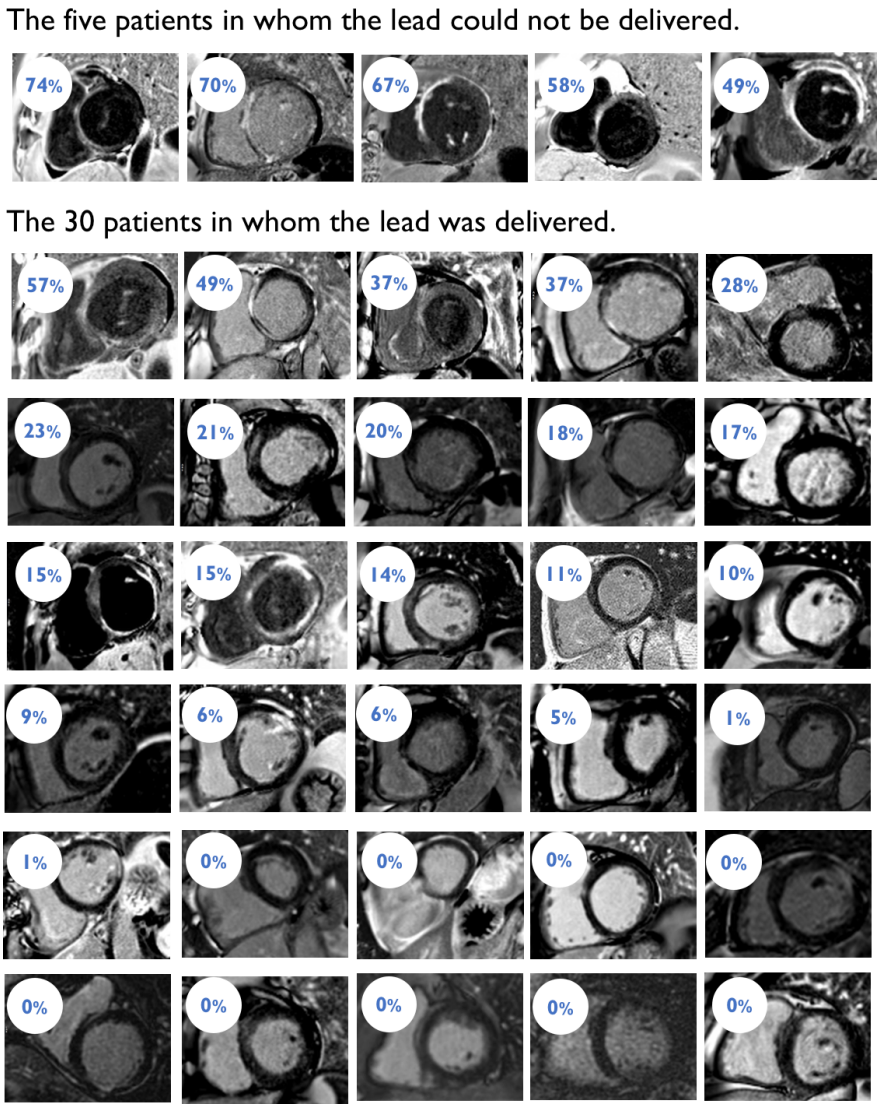

Figure 3. Images of basal septum in all 35 patients. In each group patients are ordered from most to least scar extent in the basal septum.

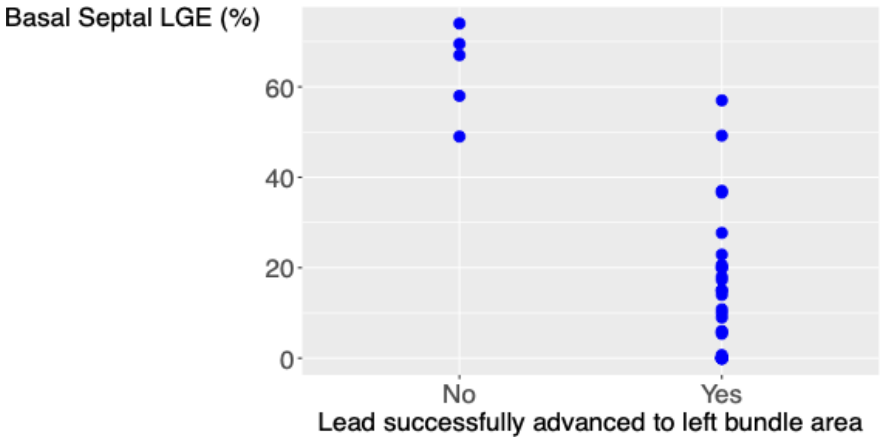

Figure 4. Basal septal LGE (%) extent in the basal septum comparing cases where lead advancement was achieved to those where it was not. A significantly higher burden of basal septal scar was found in patients where leave advancement was not successful compared to those where it was successful.

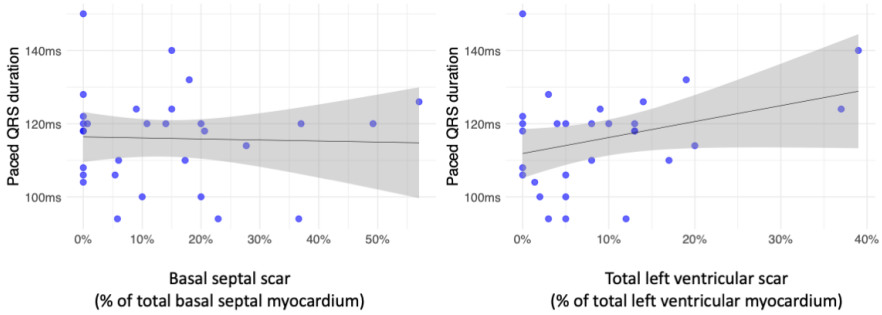

Figure 5 . The correlation between paced QRS duration achieved by left bundle area pacing and basal septal scar burden (*left*) and total scar burden (*right*) in patients where lead advancement was possible. The left bundle was captured in everyone, there was no correlation between paced QRS duration and burden of scar in the basal septum.

Hosted file

`image6.emf` available at https://authorea.com/users/495048/articles/576896-septal-scar-predicts-failure-of-lead-advancement-to-the-left-bundle-area

Graphical abstract image. Burden of scar in the basal septum assessed using late gadolinium enhancement (LGE) predicts failure of the lead to penetrate the septum deep enough to reach the left bundle area. Middle figure shows two cardiac MRI images of the basal septum with LGE left; no scar and right high scar burden (white color). Once the lead is advanced there is no correlation between the paced QRS duration and basal septal scar burden.