Mapping and ablation of atrial tachyarrhythmias : from signal to substrate

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chapter 7

Epicardial High Density Mapping of Bachmann's Bundle in Humans with Chronic Atrial Fibrillation

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Abstract

Introduction: Animal studies have shown that bachmann's bundle (BB) is essential for development of multiple reentrant circuits perpetuating atrial fibrillation (AF). Direct mapping of BB in humans has sofar not been performed. In this study, high density epicardial mapping of BB was performed in order to study conduction characteristics of fibrillation waves across BB during chronic AF in humans.

Methods: Epicardial mapping studies of BB were performed in patients (n = 8, 66 ± 12 yrs, 3 male) with chronic AF during cardiac surgery for mitral valve disease with a template containing 60 unipolar electrodes (inter-electrode distance 1.5 mm). Ten seconds of AF were recorded from the middle (MBB), right (RBB) and left site of BB (LBB). Isochronal maps (n = 145 ± 65) were off-line constructed to analyse patterns of activation. For each mapping site, AF cycle length (ACFL), the incidence of conduction block (CV < 7.5 cm/s) and the incidence of fractionated fibrillation potentials was determined.

Results: For all patients, there was no difference in the incidence of single waves propagating without conduction delay (31 ± 38 (0-90)%), single waves propagating around areas of conduction block (18 ± 14 (0-35)%) and multiple wavelets separated by areas of conduction block (38 ± 34 (0-85)%). The incidence of epicardial breakthrough was (26 ± 36%). In one patient, all maps demonstrated epicardial breakthroughs. In two patients, electrical activity at MBB was absent. In 5 patients, fibrillation waves propagated with a variable degree of complexity across BB. Electrophysiological variables are summarized in **Table 1**.

	RBB	MBB	LBB
AFCL (ms)	234 ± 73 (143-319)	180 ± 20 (152-203)	192 ± 30 (142-228)
conduction block (%)	8 ± 12 (0-12)	* 18 ± 13 (0-36)	7 ± 7 (0-18)
Fractionation (%)	22 ± 20 (0-51)	19 ± 13 (0-32)	13 ± 18 (0.15-48)

* p = 0.04

Conclusion: In humans with chronic AF, there is an inter-individual variation in patterns of activation across BB. This is reflected by a variable degree in conduction block and fractionation of fibrillation potentials. Hence, the role of BB during AF may vary between patients and it can therefore be expected that the effects from therapies e.g. ablation or preventive pacing may also differ between patients.

Introduction

Bachmann's bundle (BB) is a band of muscular fibers originating from the crest of the crista terminalis near the superior cavoatrial junction, crossing the left atrial roof and diverging anteriorly to the left atrial appendage and posteriorly between the pulmonary veins.[1;2] Anatomical and electrophysiological characteristics of BB are different from the surrounding atrial myocardium.

During sinus rhythm, BB is the main route of interatrial conduction.[1] Conduction block at BB results in widening and prolongation of the P wave. In the goat model, the refractory period at mid BB was longer compared to right and left atrial sites.[3] Premature beats were blocked at the mid BB, gave rise to reentry and subsequently initiated atrial fibrillation (AF). Kumagai et al. demonstrated in the canine sterile pericarditis model that during induced AF BB is critical for development of multiple unstable reentrant circuits perpetuating AF.[4] Ablation of BB terminated AF, suggesting that BB was either a part of the reentry circuit or only a pathway for wavefronts to pass from one atrium to another.

In humans, the role of BB in arrhythmogenesis of atrial tachyarrhythmia has only been evaluated indirectly by endocardial mapping. The assumed endocardial entrance site of BB in the right atrium is a preferential area of conduction delay in patients with AF.[5] Pacing at this site shortens total atrial activation time and prevents progression from paroxysmal AF to chronic AF.[6-8] *Direct* mapping of BB has sofar not been performed in humans.

In this study, we analysed conduction characteristics of fibrillation waves across BB in patients with chronic AF (CAF) by performing epicardial high density mapping of BB during open chest surgery.

Methods

Study Population

Epicardial mapping of BB was performed in patients with CAF (n = 8, 66 ± 12 yrs, 3 male) during cardiac surgery for mitral valve disease and/or surgical isolation of the pulmonary veins. Six patients had mitral valve disease and one patient also had coronary artery disease. Lone AF was present in 2 patients. AF was permanent for at least one year.
At the moment of cardiac surgery, none of the patients used anti-arrhythmic drugs.

Data Acquisition

If patients were in sinus rhythm at the onset of the mapping procedure, AF was induced by fixed rate pacing using electrodes sutured to the right atrial appendage. Epicardial mapping of BB was performed before patients were put on cardiopulmonary bypass. The mapping device was a 1cm^2 electrode containing 60 unipolar teflon-coated silver electrodes with a diameter of 0.3 µm and an inter-electrode distance of 1.5 mm (**Figure 1**). BB was mapped by shifting the mapping array from the superior cavoatrial junction to the base of the left atrial appendage. At each site, recordings of 10 seconds were made using a computerized mapping system. A silver plate was positioned inside the thoracic cavity and served as an indifferent electrode. Sixty simultaneously acquired unipolar epicardial fibrillation electrograms and the surface ECG lead were stored on hard disk after amplification (gain 1000), filtering (bandwidth 1-500 Hz), sampling (1 KHz) and analogue to digital conversion (12 bits).

Data Analysis

Fibrillation maps were off-line constructed by measuring local activation times at each electrode. The moment of local activation was detected by automatically marking the steepest negative deflection of fibrillation potentials. All annotations were visually verified and edited if necessary. AF cycle length (AFCL) was determined by measuring intervals between consecutive depolarisations at each electrode. For each mapping site, median AFCL was assessed from fibrillation intervals recorded by all 60 unipolar electrodes during 10 seconds of AF. Fibrillation potentials were classified according to the criteria described in chapter 6. At each mapping site, the incidence of single –, short double –, long double –, fractionated potentials and continuous electrical activity was determined. In case of a fractionated fibrillation potential or continuous electrical activity, the total duration (fractionation duration), defined as the time between the steepest negative deflection of the first and last component, was measured.
At every electrode, local conduction velocity during AF was assessed by constructing local conduction velocity vectors in areas of 3 x 3 electrodes. To study local dissociation in conduction, inter-electrode conduction delays were used to determine the incidence of local conduction block (inter-electrode conduction time ≥ 20 ms, corresponding with a conduction velocity ≤ 7.5 cm/s).

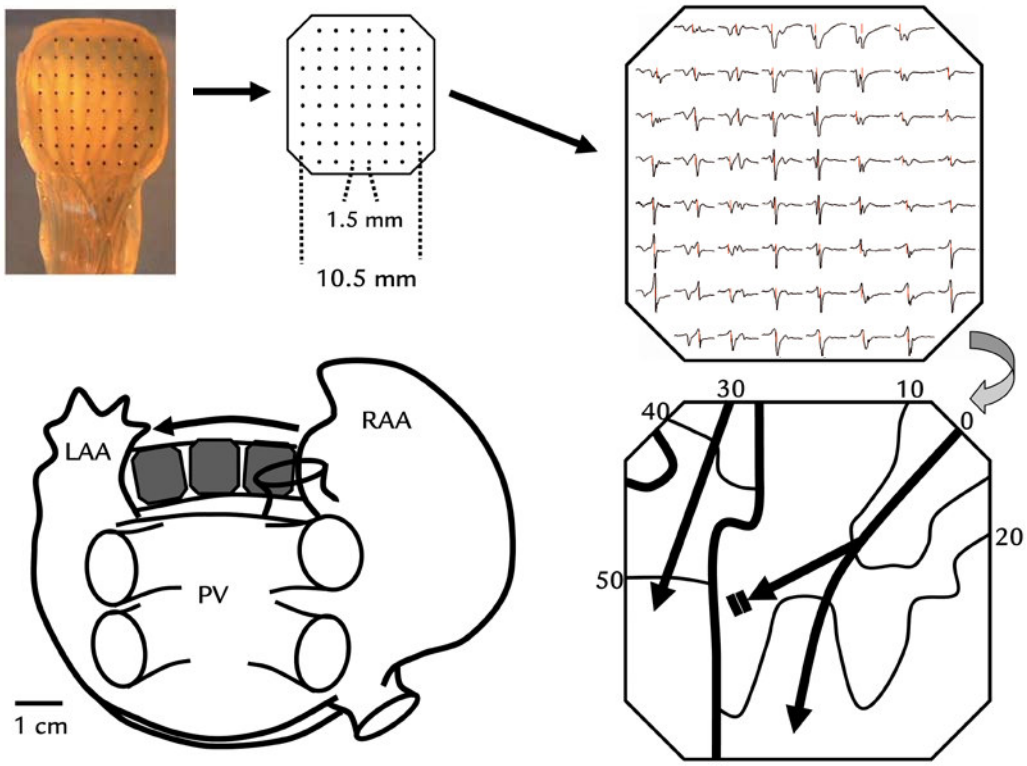

Figure 1.
Mapping of BB was performed with an electrode containing 60 unipolar electrodes (diameter of 0.3 µm) with an inter-electrode distance of 1.5 mm. BB was mapped by moving the electrode from the superior cavoatrial junction to the anterior left atrial wall. At each site, 60 electrograms were simultaneously recorded during 10 seconds of AF. Fibrillation maps were off-line reconstructed for analysis of patterns of activation.

Fibrillation maps were used to classify patterns of activation. For this purpose, the incidence of 1) single waves propagating without conduction delay, 2) single waves propagating around an area of conduction block, 3) two or more wavelets separated by areas of conduction block and 4) epicardial breakthroughs (emerging of a new wavefront in the middle of the mapping area which could not be explained by wavefronts travelling in the epicardial plane) was determined.

Statistical Analysis

All data are expressed as mean ± standard deviation, range or percentage. Students T-tests were used to evaluate intra-atrial differences between electrophysiological variables. A probability level of 5% was considered statistically significant.

Results

Electrophysiological characteristics of the various mapping sites of BB are summarized in Table 1. The number of recording sites along BB ranged from 2 to 4. Mapping of BB required 2 positions in two patients, 3 positions in five patients and 4 positions in one patient. In two patients, the right and left side of BB were separated by an area from which no electrical activity could be recorded.

Atrial Fibrillation Cycle Length

Figure 2 shows the median AF cycle length at different mapping positions for each patient individually. A total of 4485 ± 5563 fibrillation intervals were measured. Median AF cycle length ranged from 142 to 319 (199 ± 45) ms. There were no differences in fibrillation intervals obtained from the right, left and middle side of BB. Hence, there was no frequency gradient across BB.

Fractionation of Fibrillation Potentials

In Figure 3, samples of fibrillation potentials obtained from the middle of BB demonstrate a variable degree of fractionation. The incidence of fractionated potentials at all mapping positions for every patient separately is shown in the lower left panel of Figure 3. The incidence of fractionated fibrillation potentials along BB ranged from 0.15 to 51 (21 ± 17)%.

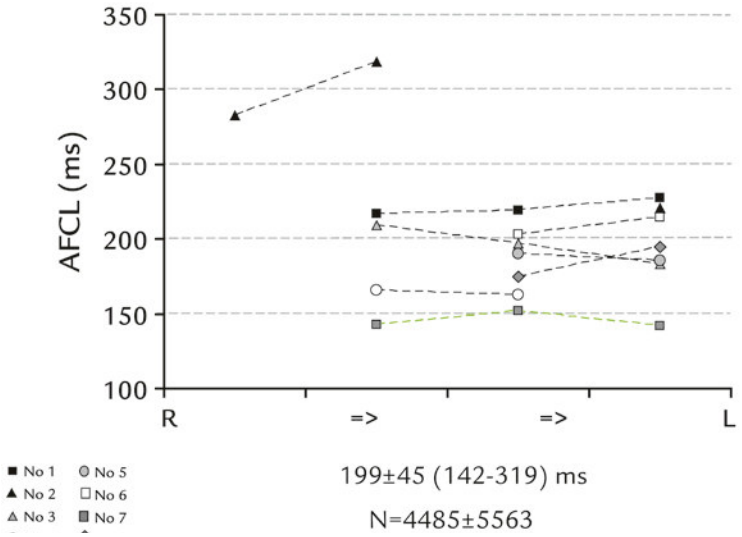

Figure 2.
Median AF cycle length at different mapping sites from the right (R) to the left (L) side along BB for each patient individually. There was no dominant frequency gradient from the right to the left side or vice versa.

Table 1. **Electrophysiological characteristics of BB during human CAF.**

	AFCL (ms)			FP (%)			CB (%)		
	mean/ sd	min	max	mean/sd	min	max	mean/sd	min	max
1	223 ± 8	217	228	2 ± 3	0	5	2 ± 2	0	3
2	274 ± 50	221	319	4 ± 4	0	9	0 ± 1	0	1
3	196 ± 13	183	209	29 ± 12	16	40	13 ± 5	7	18
4	165 ± 2	163	166	38 ± 17	26	51	12 ± 3	10	15
5	188 ± 3	186	190	27 ± 12	18	36	16 ± 0	16	17
6	184 ± 16	172	195	13 ± 6	8	17	2 ± 3	0	4
7	146 ± 6	142	152	26 ± 23	2	47	20 ± 17	1	32
8	209 ± 8	203	215	20 ± 28	0	39	18 ± 25	0	36

AFCL = atrial fibrillation cycle lenght, FP = fractionated potentials, CB = conduction block.

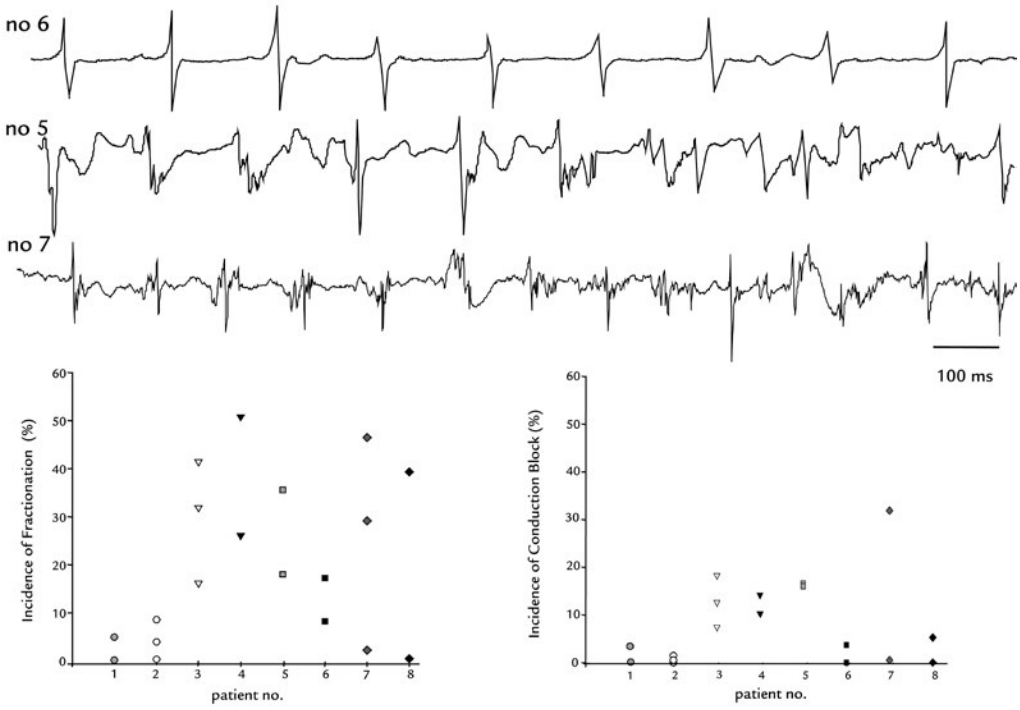

Figure 3.

Typical examples of fibrillation potentials recorded from the middle of BB demonstrating inter-individual variation in the morphology of fibrillation potentials. Lower panel: the incidence of fractionated potentials (lower left panel) and conduction block (lower right panel) at each mapping site along BB for each patient individually.

At the middle of BB, fractionated potentials were as frequently recorded as at the borders of BB (25 ± 11% versus 19 ± 19%, p = 0.3). A higher degree of fractionation was related with a shorter median AFCL (r = -.056, p = 0.01).

The incidence of conduction block at the various mapping sites is shown in the lower right panel of **Figure 3**. Between patients, the incidence of conduction block varied from 0% to 36%. Comparable to the degree of fractionation, there were also regional differences in the incidence of conduction block along BB (11 ± 14%). Conduction block occurred more frequently in the middle of BB than at the borders of BB (19 ± 13% versus 7 ± 9%, p = 0.04). The degree of fractionation correlated with the incidence of conduction block (r = 0.75, p = 0.001).

Conduction Characteristics of Fibrillation Waves

Fibrillation maps (n = 145 ± 65) were constructed in order to analyse patterns of activation and preferential conduction directions. In every patient, electrical activity could not be recorded from small parts of the mapping area despite ensurance of good contact between BB and the mapping electrode at one of more mapping sites.

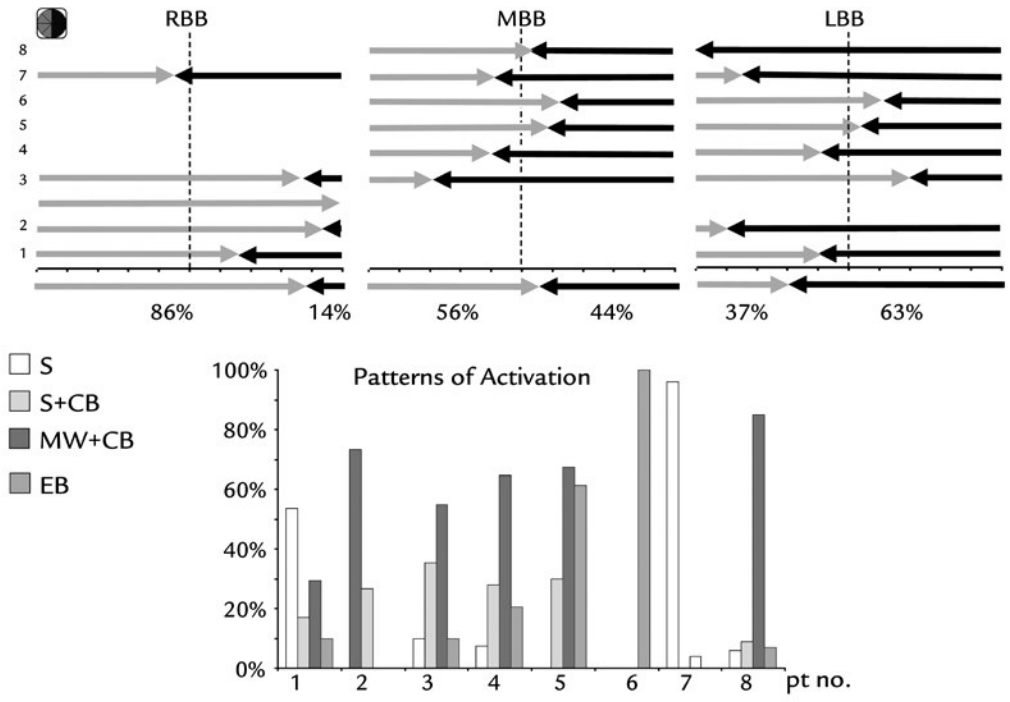

Figure 4.

Upper panel: main direction of propagation at the right side (RBB), middle (MBB) and left side (LBB) of BB. *Lower panel:* incidence of the various patterns of activation observed along BB for each patient separately.

S = single waves, S+CB = single waves and conduction block, MW+CB = multiple waves and conduction block, EB = epicardial breakthrough.

The main direction of conduction within the mapping area at the various mapping sites is shown in the upper panel of **Figure 4**. At the right side of BB, the majority of the fibrillation waves propagated from the right to the left side of the mapping area (86% versus 14%, p = 0.001). At the left side of the mapping area, most fibrillation waves traveled from the left to the right side (64% versus 37%, p = 0.04). At the middle of BB, there was no preferential conduction direction (left to right: 44% versus right to left: 56%, p = 0.25). The incidence of the different patterns of activation for each patient individually is shown in the lower panel of **Figure 4**. In the entire study population, there was no difference in the incidence of single waves propagating without conduction delay (31 ± 38 (0-90)%), single waves propagating around areas of conduction block (18 ± 14 (0-35)%) and multiple wavelets separated by areas of conduction block (38 ± 34 (0-85)%). The incidence of epicardial breakthrough was (26 ± 36 (0-100)%).

Analysing the patterns of activation for each patient along BB separately, several patterns of activation were observed (**Figure 5**). In one patient (no.6), the mapping area appeared to be activated simultaneously from multiple directions and there was no clear activation direction. This pattern of activation was similar across entire BB (upper panel). In two

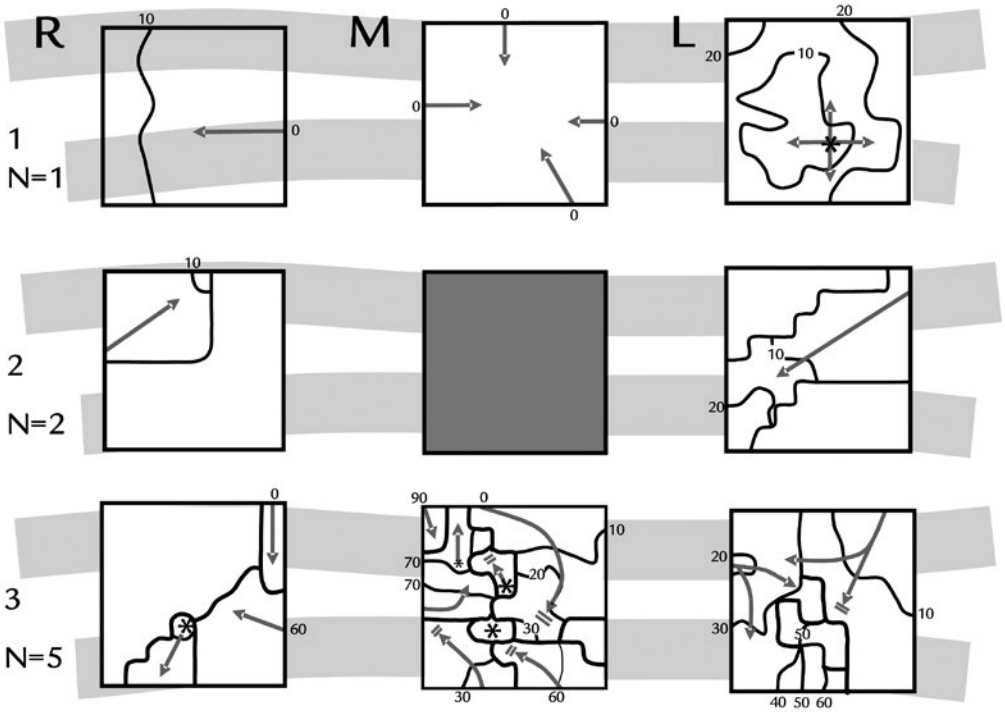

Figure 5.

Representative examples of successive isochronal maps obtained from 3 different patients demonstrating typical patterns of activation observed at BB.

Isochronal maps were drawn at 10 ms intervals, arrows show main activation direction, thick black lines represent areas of conduction block and * indicates the site of origin of epicardial breakthrough of fibrillation waves.

patients (pt no. 1 and 2), fibrillation waves propagated from either the right or left atrium towards the middle of BB (middle panel) and the majority of the waves propagated at high conduction velocities without encountering areas of conduction block. At the middle of BB, electrical activity could not be recorded (grey area, electrically silent tissue).
In the remaining patients, the fibrillation waves propagated across BB with a variable degree in the complexity of the patterns of activation (lower panel). Episodes with multiple co-existing wavelets and epicardial breakthroughs separated by areas of conduction block were interspersed with single broad wavefronts propagating without conduction delay. Figure 6 shows sixteen consecutive fibrillation maps constructed from the middle of BB of patient no. 4 demonstrating beat-to-beat variation in the complexity of activation. Areas of conduction block are indicated by thick black lines and epicardial breakthroughs are marked with an asterix (*). The mapping area is activated by wavefronts entering from different directions or by epicardial breakthroughs. Also, parts of the mapping area were

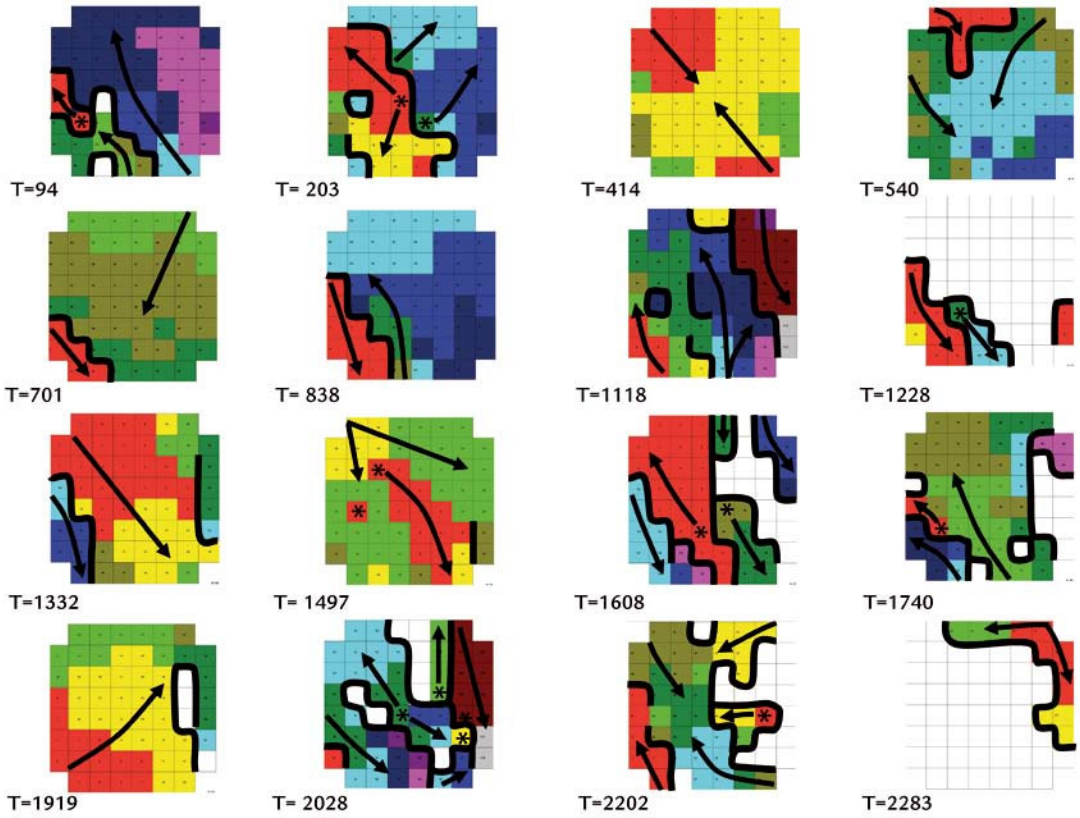

Figure 6.
Sixteen consecutive color coded fibrillation maps constructed from the middle of BB. Patterns of activation in this area are characterized by a beat-to-beat change in activation direction, epicardial breakthroughs and local conduction block. In most fibrillation maps, parts of the mapping area were not activated due to conduction block of fibrillation waves.

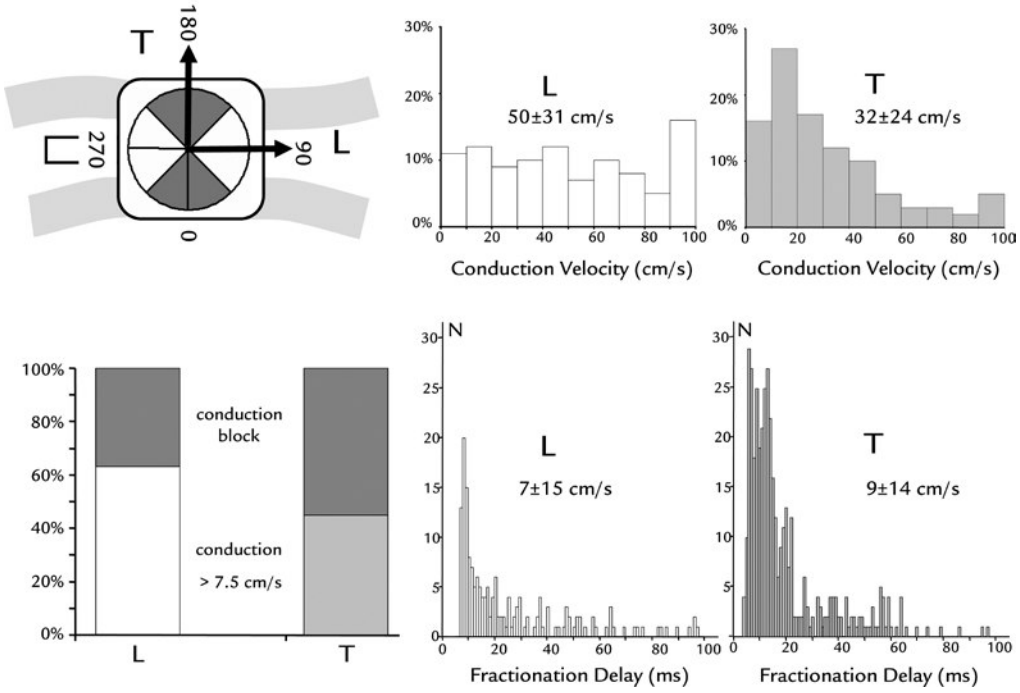

Figure 7.

Relation between propagation direction conduction velocity (*upper right panel*), the incidence of conduction block and (*lower left panel*) fractionation delay of fibrillation potentials (*lower left panel*) during 10 seconds of AF. Recordings were obtained from the same patient demonstrated in figure 7.

not activated due to conduction block of fibrillation waves. Corresponding directional differences in conduction characteristics during 10 seconds of AF are demonstrated in Figure 7. Conduction direction was correlated with the incidence of conduction block, conduction velocity and fractionation delay. For this purpose, differences in longitudinal (white area, angle between 45-≤135° and 225-≤315°) and transverse (grey angle between 136-≤224° and 224-≤44°) propagation direction were evaluated. Comparing longitudinal and transverse conduction, conduction velocity in the transverse direction was slower (32 ± 24 cm/s versus 50 ± 31 cm/s, p = 0.001) and conduction block occurred more frequently (55% versus 37%). Prolonged conduction delay in the transverse direction was also reflected by a longer fractionation delay (9 ± 14 cm/s versus 7 ± 15 cm/s, p = 0.01). Similar directional differences in conduction were also found in patient no. 1 and 3. However, no differences in transverse and longitudinal propagation could be found in two patients with slow conduction and a high incidence of conduction block in both directions (patient no. 5 and 7). In the remaining patients (patient no. 2, 6 and 8) differences in transverse and longitudinal conduction characteristics could not be calculated due to either the low incidence of conduction block or a local preferential conduction direction.

Discussion

The goal of this study was to analyze conduction characteristics of fibrillation waves across BB during CAF in humans by performing epicardial high density mapping. The major finding of this study is that patterns of activation differed considerably between patients, with a variable degree of heterogeneity in conduction. In some patients, electrical activity was absent in the middle of BB. These findings indicate that the role of BB during CAF may also differ between patients.

Frequency Gradient

Spectral analysis of optical recordings obtained from isolated sheep heart during acetylcholine induced AF demonstrated the presence of stable microreentrant sources located in the left atrium. [9] Waves emerging from these high frequency sources propagated across interatrial pathways such as BB or infero-posterior pathways to the right atrium. In the right atrium, there was a frequency dependent breakdown of fibrillation waves resulting in fibrillatory conduction in the right atrium. This pattern of activation during AF gave rise to a frequency gradient across BB.

In our study population, there was no consistent left-to-right or right-to-left conduction and there was also no frequency gradient across BB. Instead, the majority of the fibrillation waves entered from either the right or left side of BB and propagated towards the middle.

At several mapping sites, electrical activity was only recorded in a part of the mapping area. This is most likely the result of the trapezoidal shape and small size of BB relative to the mapping electrode. However, absence of electrical activity can also be explained by fatty-fibrosis replacement of myocardial tissue which has been described in patients with AF. In two patients, electrical activity could not be recorded from the middle of BB. This could be due to absence of BB in some humans, as shown by examination of post-mortem hearts. [10]

Local Inhomogeneity in Conduction

Consistent with local inhomogeneity in conduction, the incidence of fractionated potentials in this study population also varied considerably. In some individuals, fractionated fibrillation potentials were even rarely recorded. There was not only an inter-individual variation in the degree of fractionation, but there were also regional differences in fractionation along BB. Fractionation at BB was associated with a shorter median AFCL, suggesting a relation between refractoriness and fractionation. Experimental studies have demonstrated that the refractory period at BB is relative long compared to the remainder of the atria. Fibrillation waves propagating across BB may encounter tissue which is still refractory; this results in local conduction abnormalities and subsequent fractionation of fibrillation potentials. Fractionation may also be due to non-uniform anisotropy, slow

discontinuous conduction or longitudinal dissociation in conduction. In addition, entrances of multiple wavelets from the intra-atrial septum, the right and left atrial appendages may further enhance the degree of fractionation.
Experimental studies are inconsistent to whether unidirectional conduction block in non-uniform anisotropic tissue preferentially occurs in longitudinal or transverse conduction direction. In this study, the incidence of fractionated fibrillation potentials and conduction block occurred more frequently in the transverse propagation direction in patients with a moderate degree of local conduction block. Our data could be explained by the experiments of Koura et al. [11] In their study, they demonstrated that, the spread of an electrical impulse changes from an elliptical to a square pattern of activation during ageing which was associated with a decrease in the incidence of conduction block in the longitudinal direction and an increase in the transverse direction. In the other patients, the incidence of conduction block was higher and conduction block in the longitudinal direction occurred as frequently as in the transverse propagation direction. It could be hypothesized that the myocardial structure of BB in these patients is completely distorted, which results in conduction block in all directions and hence diminishes directional differences in conduction.

The Role of Bachmann's Bundle during Chronic AF

Animal studies showed that BB is critical for development of multiple, unstable reentrant circuits during AF and that ablation of BB terminated AF. [4] Based on this study, it was suggested that BB was either a part of the reentry circuit or only a pathway for wavefronts to pass.
In patients with a high incidence of conduction block, BB could be an area perpetuating AF. However, it is likely that in the electrical and/or structural remodeled atria of aged patients with chronic AF more areas can perpetuate AF. To confirm whether BB is a perpetuator of AF, electrophysiological properties of this area have to be compared with the remainder of the atria. Hence, more extensive mapping studies are required to identify areas perpetuating AF.
BB could also serve as a crucial pathway of conduction for fibrillation waves propagating from one atria to another giving rise to multiple reentering wavelets. Yet, patterns of activation supporting this assumption have been observed in only one patient.
In this patient, the mapping area appeared to be activated simultaneously from multiple directions and there was no clear activation direction. Frequently, epicardial breakthroughs excited the entire mapping area. This pattern of activation could be due to propagation of fibrillation waves at high velocities across BB or 3-dimensional conduction through the inter-atrial septum.

Conclusion

In humans with CAF, there is an inter-individual variation in patterns of activation across BB. This is reflected by a variable degree in conduction block and fractionation of fibrillation potentials. Hence, the role of BB during AF may vary from patient to patient and it can therefore be expected that the effects from therapies e.g. ablation or preventive pacing may also differ between patients.

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