Mapping and ablation of atrial tachyarrhythmias : from signal to substrate

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chapter

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Voltage and Activation Mapping: How the recording technique affects the outcome of catheter ablation procedures in patients with congenital heart disease

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Abstract

Introduction: Endocardial mapping is mandatory prior to radiofrequency catheter ablation (RFCA). Mapping can be performed using either unipolar or bipolar recordings. Impact of the recording technique used was studied in patients with and without structural heart disease using the 3-D electro-anatomical CARTO™ mapping system.

Methods: Patients (n = 44, 16 M, 43 ± 16 yrs) referred for RFCA of atrial flutter (AFL, n = 18), focal atrial tachycardia (FAT, n = 4), atrio-ventricular nodal reentrant tachycardia (AVNRT, n = 5) or scar related atrial reentrant tachycardia (IART, n = 17) were studied. Voltage- and activation maps were constructed. Unipolar and bipolar voltage distribution in the different groups was studied to establish a cut-off voltage value to facilitate delineation of scar tissue.

Results: Electrograms were recorded during tachycardia (FAT: n = 246, CL = 449 ± 35ms, AVNRT: n = 182, CL = 359 ± 47ms, AFL: n = 1164, CL = 255 ± 56ms, IART: n = 2431, CL = 280 ± 74 ms). Unipolar voltages were > bipolar voltages ($p < 0.001$). Unipolar voltages ≤ 1.0 mV were equally distributed in both AFL and IART patients. Bipolar voltages ≤ 0.1mV were only found in patients with IART, and subsequently 0.1mV was used as cut-off value to delineate scar tissue. No unipolar cut-off value could be established. Timing of unipolar and bipolar local activation was correlated in all patient groups.

Conclusion: The recording technique used has considerable impact on reconstruction of reentrant pathways and on the outcome of RFCA. In general, unipolar and bipolar recordings provide complementary information; however, only bipolar recordings allow voltage-based scar tissue delineation in patients with congenital heart disease.

Introduction

Radiofrequency catheter ablation (RFCA) is an established treatment modality for different arrhythmias.[1-4] Target sites for RFCA are identified by endocardial mapping of the activation sequence, the potential distribution, and/ or the morphology of the recorded signals. Especially in patients with surgically corrected congenital heart disease and atrial reentrant arrhythmias, identification of target sites is challenging as reentrant circuits are complex with multiple entrances and exit sites.[5] Target sites in these patients are often slow conducting narrow isthmuses bordered by areas of scar tissue.[6] Voltage criteria have been developed to allow discrimination of these slow conducting pathways from surrounding scar tissue areas.[7] The introduction of 3-D mapping systems facilitated the time consuming and difficult process of reconstruction of complex reentrant circuits.[8-11] However, accurate determination of local activation time and of signal amplitude is still difficult and to some degree operator dependent.[12,13] Recordings are affected by different factors like enhanced (non-uniform) anisotropy and/or the presence of scar tissue.[14-16] Furthermore, the recording technique applied (unipolar- or bipolar recordings), mapping catheters used (type of electrodes, electrode spacing), and filter settings of the amplifiers have considerable influence on the resulting activation- and voltage maps.[17-22] Most studies comparing unipolar and bipolar signals are based on animal experiments or computer simulation studies, and only a few clinical studies have been reported.[13-15] We evaluated the effects of the recording technique applied on voltage- and activation map reconstruction in 4 groups of patients with and without congenital heart disease, using the 3-D CARTO™ mapping system.

Methods

Forty-four patients (43 ± 16 yrs, ± 16 male, **Table I**) referred for RFCA of focal atrial tachycardia (FAT), A-V nodal reentrant tachycardia (AVNRT), atrial flutter (AFL) or intra atrial reentrant tachycardia (congenital heart disease patients, IART) were included. Prior to ablation, patients underwent cardiac evaluation including 24 hour Holter monitoring, echocardiography and a diagnostic electrophysiological study. Anti-arrhythmic drugs were discontinued at least 3 days prior to ablation.

Mapping Procedure

Endocardial mapping was performed with the CARTO 3-D electro-anatomical mapping system (Biosense-Webster, USA). A 7F Navi-Star catheter (4mm tip, 2 bipolar electrode pairs, inter-electrode distance 2 mm, Biosense-Webster, USA) was used as mapping / ablation catheter. The catheter was dragged over the endocardial surface to record electrograms at different sites and to simultaneously determine the shape and volume of the atrium. A recording was only accepted and integrated in an activation or voltage map when the variability in cycle length, local activation time stability and maximum beat to beat difference of the catheter's location were < respectively 2%, 3ms, and 4mm.[7,8] These parameters, combined with impedance measurements were used to exclude signals with low amplitudes due to poor contact of the catheter's tip with the endocardial wall.[7,8] Unipolar and bipolar electrograms were recorded simultaneously. Bipolar electrograms were constructed by subtracting two unipolar electrograms (tip and distal ring electrode). All signals were filtered at 10-400Hz. Wilson's central terminal served as indifferent electrode for unipolar recordings.[9] A quadripolar 6F reference catheter (Biosense Webster, USA) was positioned into the right atrium.

Local activation time was determined automatically by marking respectively the maximum negative slope of the intrinsic deflection (unipolar recording) or maximum amplitude (bipolar recording). Markings were adjusted manually if necessary. When an unipolar or bipolar electrogram consisted of multiple deflections, the largest deflection was marked as the moment of local activation.[7,8] Color-coded activation maps were reconstructed on-line and superimposed on the anatomy. The peak-to-peak amplitude of both unipolar and bipolar electrograms was measured automatically and used to construct on-line color-coded unipolar and bipolar voltage maps. In case of fragmented electrograms, the peak-to-peak amplitude of the largest deflection was measured.

Programmed electrical stimulation applying up to three extra-stimuli (twice diastolic threshold) was performed with a constant current stimulator (Medtronic, USA).

Radiofrequency ablation

After mapping a standard radiofrequency ablation procedure was performed.[7,10,11] Radiofrequency current was applied for 60 sec. (maximum tip temperature set at 70°C, maxi-

mum output 50 Watt). Success was defined by the following factors: 1) non-inducibility of the clinical arrhythmia after the procedure; 2) the establishment of a line of conduction block over the cavo-tricuspid isthmus (AFL patients) or 3) the establishment of a line of conduction block between 2 anatomical boundaries (e.g. scar areas, IART patients).

Post procedure and follow-up

After the procedure patients were heparinized for 24 hours. An echocardiogram and a chest X-ray were obtained <24 hours after the procedure. Aspirin (80 mg) daily was administered for 3 months.

Statistical Analysis

All data were expressed as mean value ± SD. Statistical significance was defined as $P<0.05$. Pearson's correlation coefficient was used to determine the correlation between 1) the local activation time of unipolar and bipolar electrograms, and 2) the voltage of unipolar and bipolar electrograms. To test whether there was a statistically significant difference between unipolar and bipolar electrogram voltages, we used the Wilcoxon signed ranks test.

Table 1. **Patient characteristics**

Arrhythmia	**FAT**	**AVNRT**	**IART**	**AFL**
	N = 4	N = 5	N = 17	N = 18
age (yr.)	26 ± 14	44 ± 12	36 ± 9	64 ± 9
Males/Females	0/4	1/4	5/12	10/8
coronary artery disease				2
diabetes mellitus				1
coarctatio aortae				1
atrial septal defect			3	
atrio-ventricular septal defect			1	
transposition great arteries			3	
tricuspid atresia			10	

Values are number of patients unless otherwise indicated.

Table 2. **Voltage characteristics of unipolar and bipolar electrograms**

Arrhythmia	**FAT**	**AVNRT**	**IART**	**AFL**
Unipolar electrograms				
N	246	182	2431	1164
mean ± sd (mV)	3.1 ± 1.4	3.1 ± 1.2	2.1 ± 1.9	2.5 ± 1.6
minimum (mV)	2.0	1.28	0.14	0.12
maximum (mV)	8.9	9.8	9.4	9.5
Bipolar electrograms				
N	246	182	2431	1164
mean ± sd (mV)	1.8 ± 1.6	1.6 ± 1.1	0.9 ± 1.1	1.4 ± 1.5
minimum (mV)	0.12	0.22	0.03	0.11
maximum (mV)	7.8	9.4	4.6	8.9
P-value	P<0.001	P<0.001	P<0.001	P<0.001
R(voltage)	0.73†	0.73†	0.65†	0.67†
R(LAT)	0.42†	0.54†	0.14*	0.31*
CL (ms)	449 ± 35	359 ± 47	280 ± 74	255 ± 56

LAT indicates local activation time. *P* values correspond to mean amplitude. Pearson correlation coefficients are for unipolar vs bipolar voltage (R [voltage]) and unipolar vs bipolar LAT (R[LAT]).
*$P<0.01$; †$P<0.001$.

Results

All IART patients (n = 17) had surgically corrected congenital heart disease (**Table 1**). Two of 18 AFL patients (4 clockwise, 14 counter clockwise, n = 18) had ischemic heart disease. No FAT (n = 4) or AVNRT (n = 5) patients had structural heart disease. Unipolar and bipolar electrograms were recorded during FAT (61 ± 26 signals/pt, CL = 449 ± 35ms), AVNRT (36 ± 17 signals/pt, CL = 359 ± 47ms), AFL (65 ± 36 signals/pt, CL = 255 ± 56ms) and IART (143 ± 89 signals/pt, CL = 280 ± 74ms).

Voltage distribution

Although the bipolar voltage was less than the unipolar voltage (P<0.001), a significant correlation between unipolar and bipolar recordings was found in all patient groups (**Table 2**). During FAT and AVNRT (**Figure 1A and 1B**), all unipolar electrograms had an amplitude >1.0mV. However, during AFL and IART (**Figure 1C and 1D**), a large number of unipolar signals was ≤ 1.0mV (AFL: 19%, IART: 35%, **Figure 1E and 1F**). Thus, despite the absence of detectable structural heart disease in most AFL patients, the unipolar voltage distribution was different from the unipolar voltage distribution recorded in AVNRT and FAT patients and mimicked the voltage distribution found in IART patients.

The majority of bipolar electrograms recorded in patients with FAT and AVNRT (>60%) were >1.5mV (**Figure 2A and 2B**) whereas during IART and AFL (**Figure 2C and 2D**) the majority of signals was ≤1.0mV (IART: 74%, AFL: 51%). Low voltages (≤ 0.1mV) during FAT, AVNRT, and AFL (**Figure 2E, 2F and 2G**) were equally distributed, and no signals with an amplitude ≤0.1mV were recorded in any of these patients. In patients with congenital heart disease (**Figure 2H**), 16% of the signals had an amplitude of ≤0.1mV.

Voltage maps and scar tissue delineation

From the bipolar voltage distribution curves, it is clear that in normal hearts no bipolar signals with a voltage ≤0.1mV were recorded. In contrast, in congenital heart disease patients, 16% of the signals had an amplitude ≤0.1mV. Therefore, and based on previous studies, a cut-off value of 0.1mV was taken to discriminate scar tissue from viable myocardium.[7] From the unipolar voltage distribution curves it appeared that it is not possible to depict a cut-off value to discriminate scar from conducting tissue. Therefore, scar areas were delineated based on the bipolar cut-off value of 0.1mV and on bipolar recordings only. After scar tissue mapping, the scar areas were superimposed on the anatomy. Bipolar and unipolar voltage maps were constructed using the same "scar" maps. In **Figure 3**, four pairs of corresponding unipolar (left panels) and bipolar voltage maps (right panels) recorded during FAT, AVNRT, AFL and IART are shown. Large areas of scar (grey colored areas) were recorded during IART only.

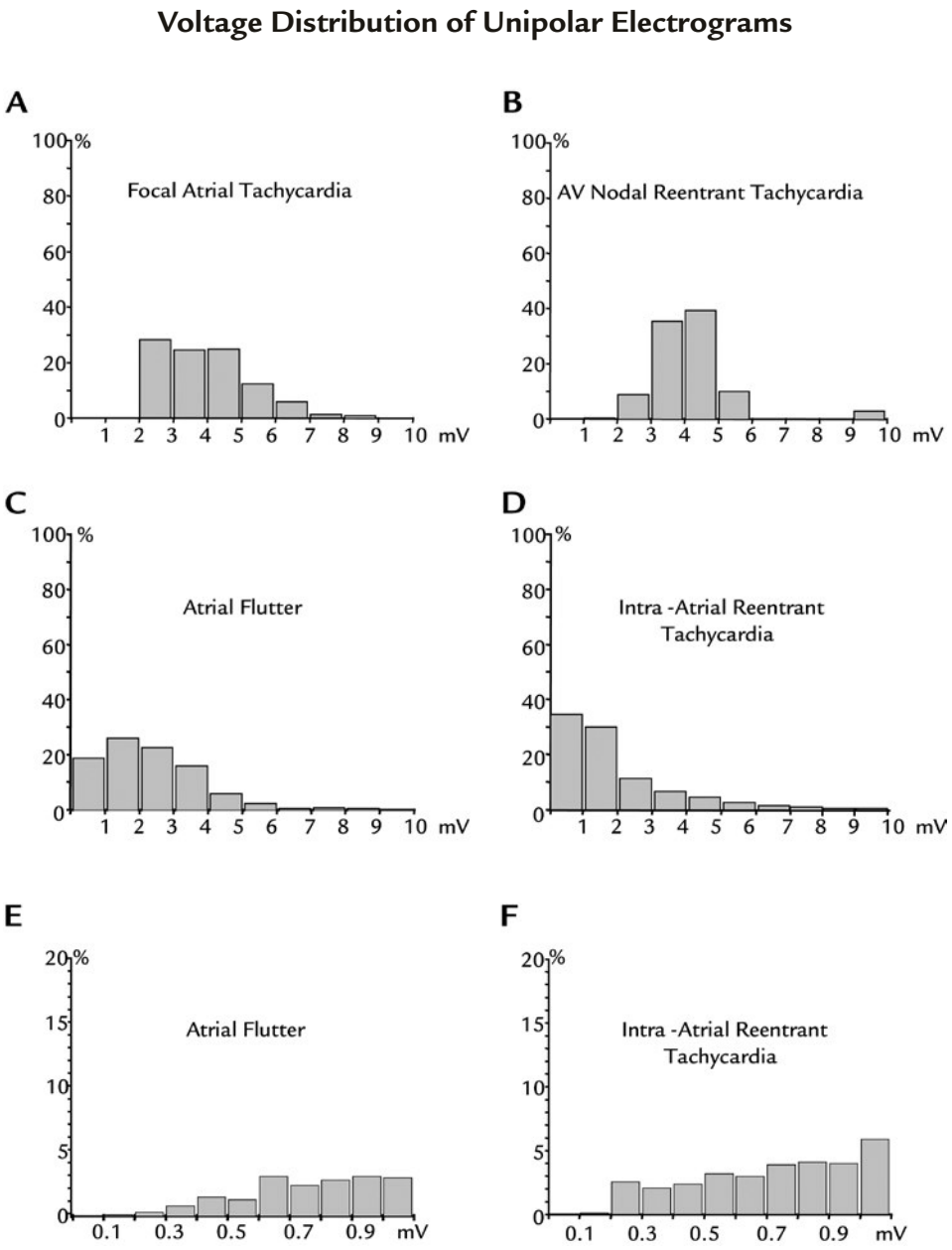

Figure 1.

Frequency distribution of unipolar electrograms. Electrograms with an amplitude < 1.0mV were only recorded in patients with AFL and IART.

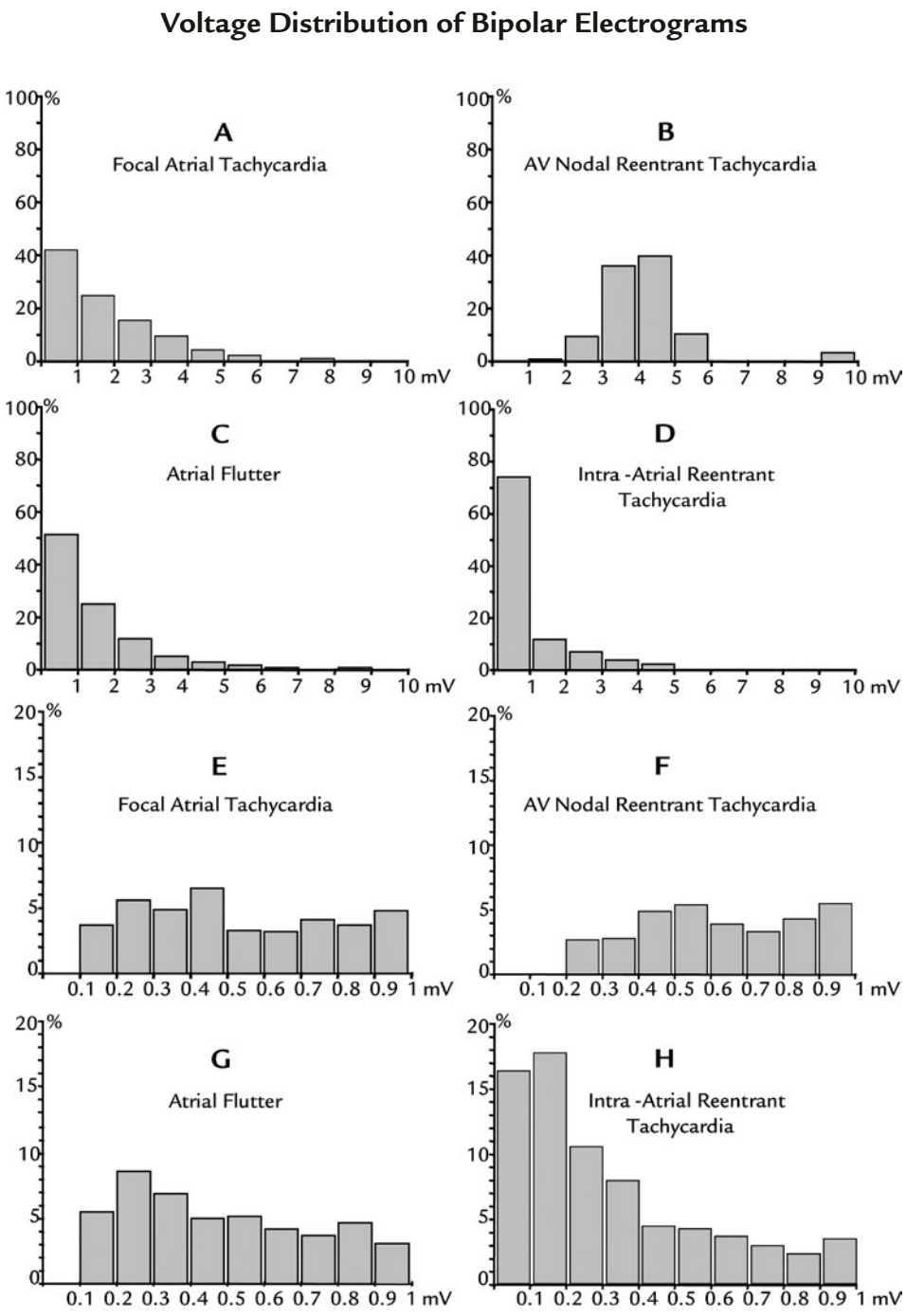

Figure 2.

Frequency distribution of bipolar electrograms. Bipolar electrograms with amplitudes ≤ 0.1mV were only recorded in patients with IART.

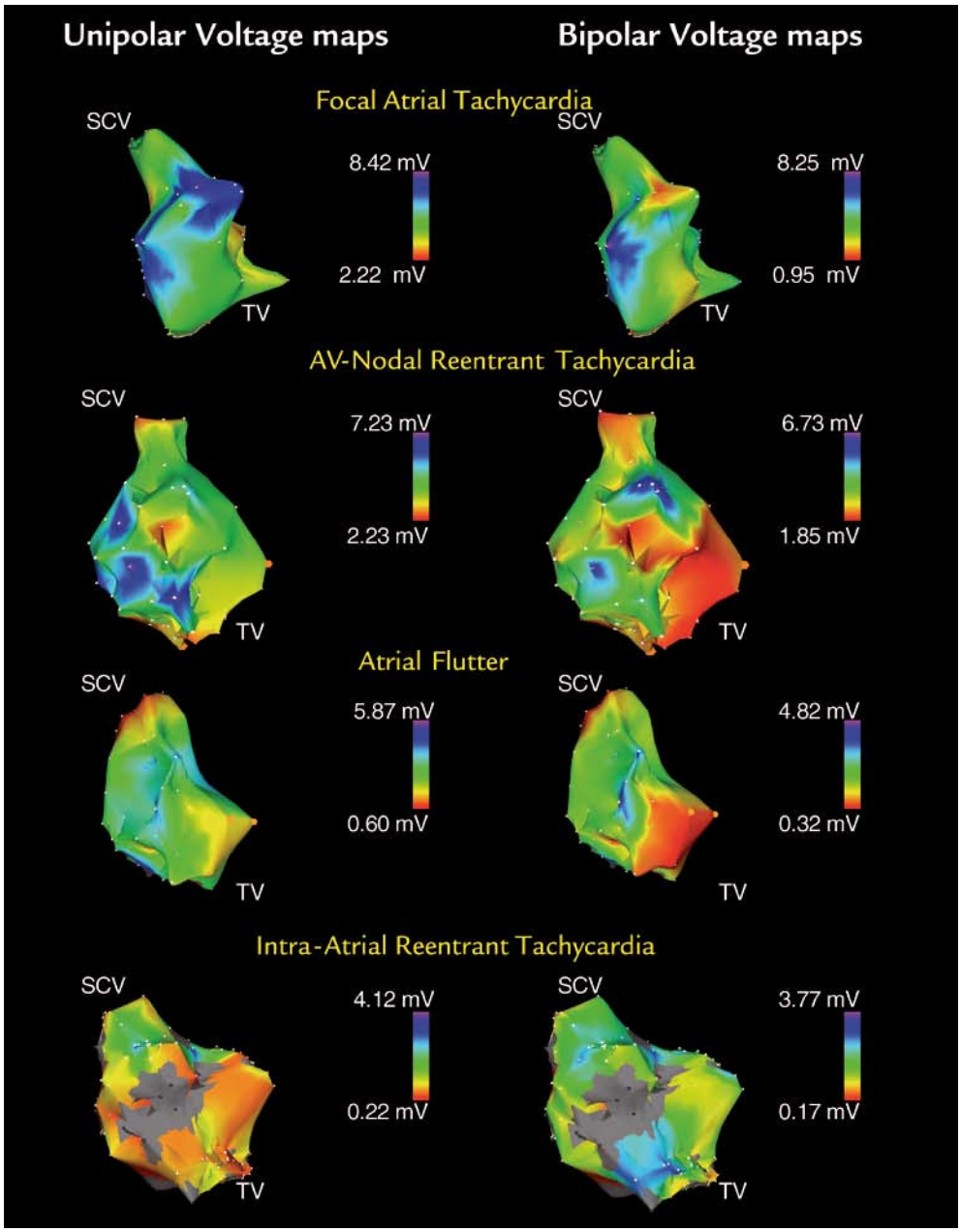

Figure 3.

Representative unipolar and bipolar voltage maps constructed during FAT, AVNRT, AFL and IART in the right atrium in 4 different patients. Voltages were color coded according to corresponding color bars. Similarity of different maps is due to use of different voltage ranges in each panel. In fact, unipolar voltages are larger than bipolar voltages in all patient groups. Scar tissue is delineated based on a bipolar cut-off value of ≤ 0.1 mV (grey colored areas). SCV = superior caval vein, TV = tricuspid valve.

Activation Mapping

In general, during FAT and AVNRT fragmentation was minimal and the local activation time could be determined automatically without manual adjustments. However, during AFL and IART, determination of local activation time was hampered by enhanced fragmentation, recorded within large areas of the endocardial surface. In case of low amplitude fragmented signals, > 85% of the automatic markings were not accurate necessitating manual adjustments. Consequently, differences in timing of unipolar and bipolar activation occurred. Despite these problems a weak but significant correlation between unipolar and bipolar activation times was found in all patient groups (Table 2). Because most signals during FAT did not show fragmentation, only minimal differences between unipolar and bipolar activation maps were found (Figure 4, left panels). Also during AFL (Figure 4, right panels), most sites only show minimal differences in timing between unipolar and bipolar recordings. However, increased fragmentation, in the area near the

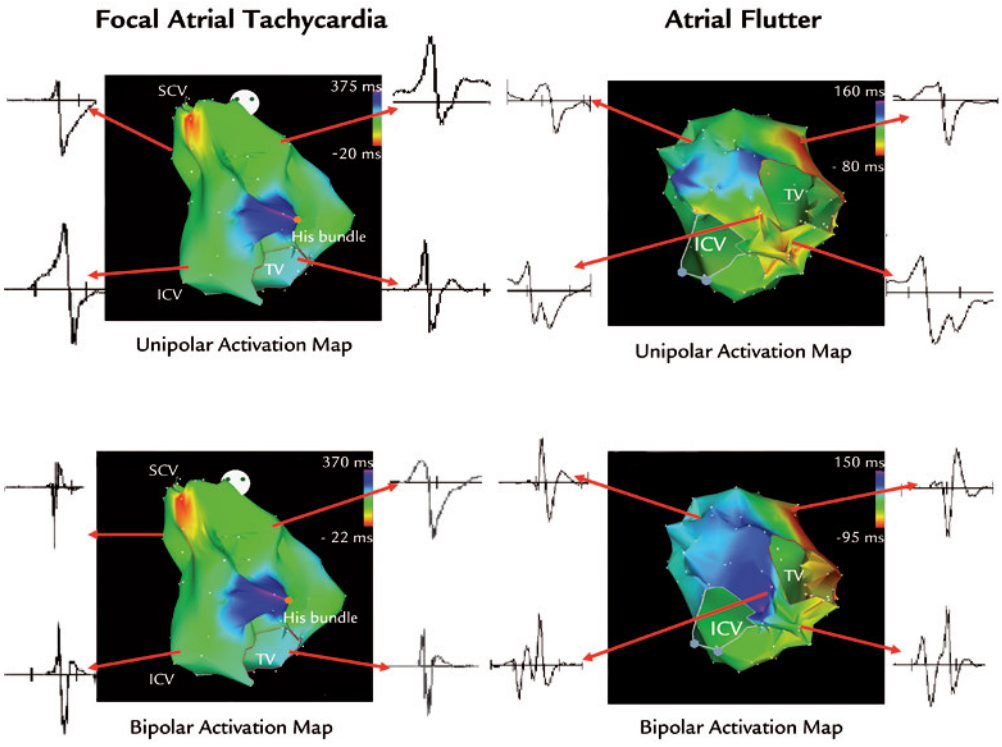

Figure 4.

Unipolar and bipolar activation maps constructed during FAT (left, CL_390 ms) and AFL (right, CL_250 ms) in anteroposterior and caudal view, respectively. Examples of electrograms are shown outside activation maps. Differences in local activation time were mainly present in areas from which fragmented electrograms were recorded. TV indicates tricuspid valve; ICV, inferior caval vein.

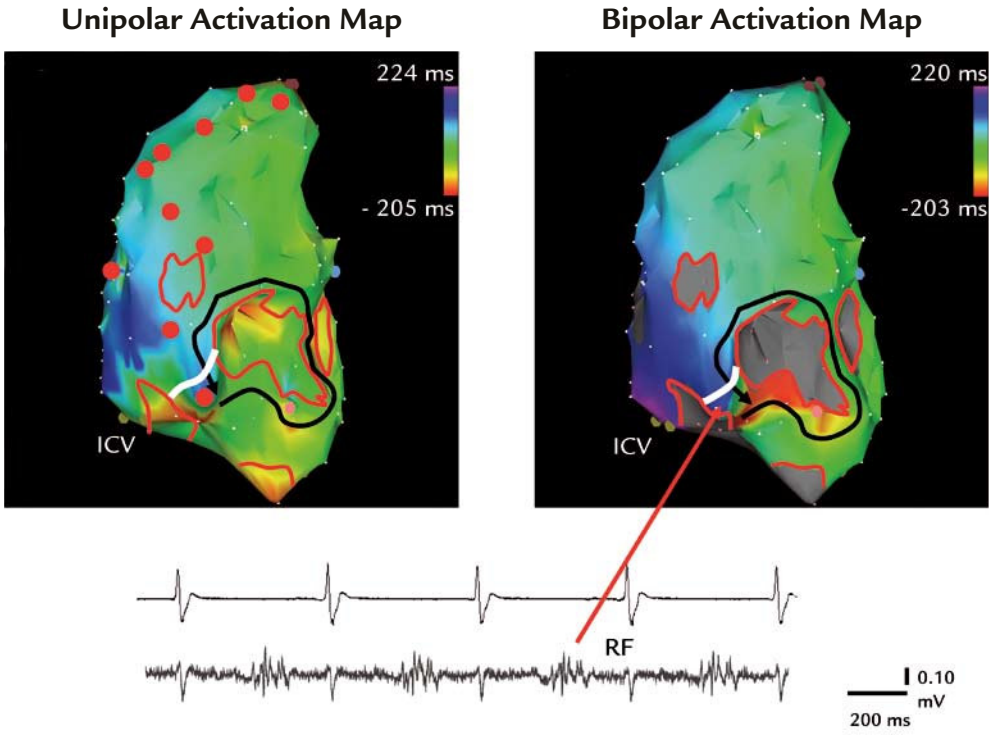

Figure 5.
Color coded unipolar and bipolar activation map of the right atrium constructed during IART (patient after Fontan's procedure, antero-posterior view). Arrow indicates direction of activation wavefront propagating around scar tissue. The red dots depicts sites with a difference in local activation time between unipolar and bipolar signals of > 20ms. See text for explanation. ICV = inferior caval vein, RF = successful ablation site.

cavo-tricuspid isthmus did result in differences between the unipolar and bipolar activation maps. During IART (**Figure 5**), differences between unipolar and bipolar activation maps due to enhanced fragmentation were even more prominent. Delineation of scar (grey colored areas) using a cut-off value of 0.1mV resulted in a few large areas of scar tissue (bipolar activation map). These scar zones were superimposed on the anatomy and used also during analysis of the unipolar activation map (red encircled areas).
Ablation aimed at connecting the 2 scar areas resulted in termination of the arrhythmia (white line). Although the unipolar and bipolar map look similar at some sites differences between the unipolar and bipolar activation time was >20 ms (red dots) hampered detailed reconstruction of the reentrant pathway. In this case, the reentrant pathway was reconstructed with only bipolar electrograms, because they were less distorted by far-field electrical activity.
Far-field electrical events may impede precise measurement of activation times, especially in low amplitude areas during IART (**Figure 6**).

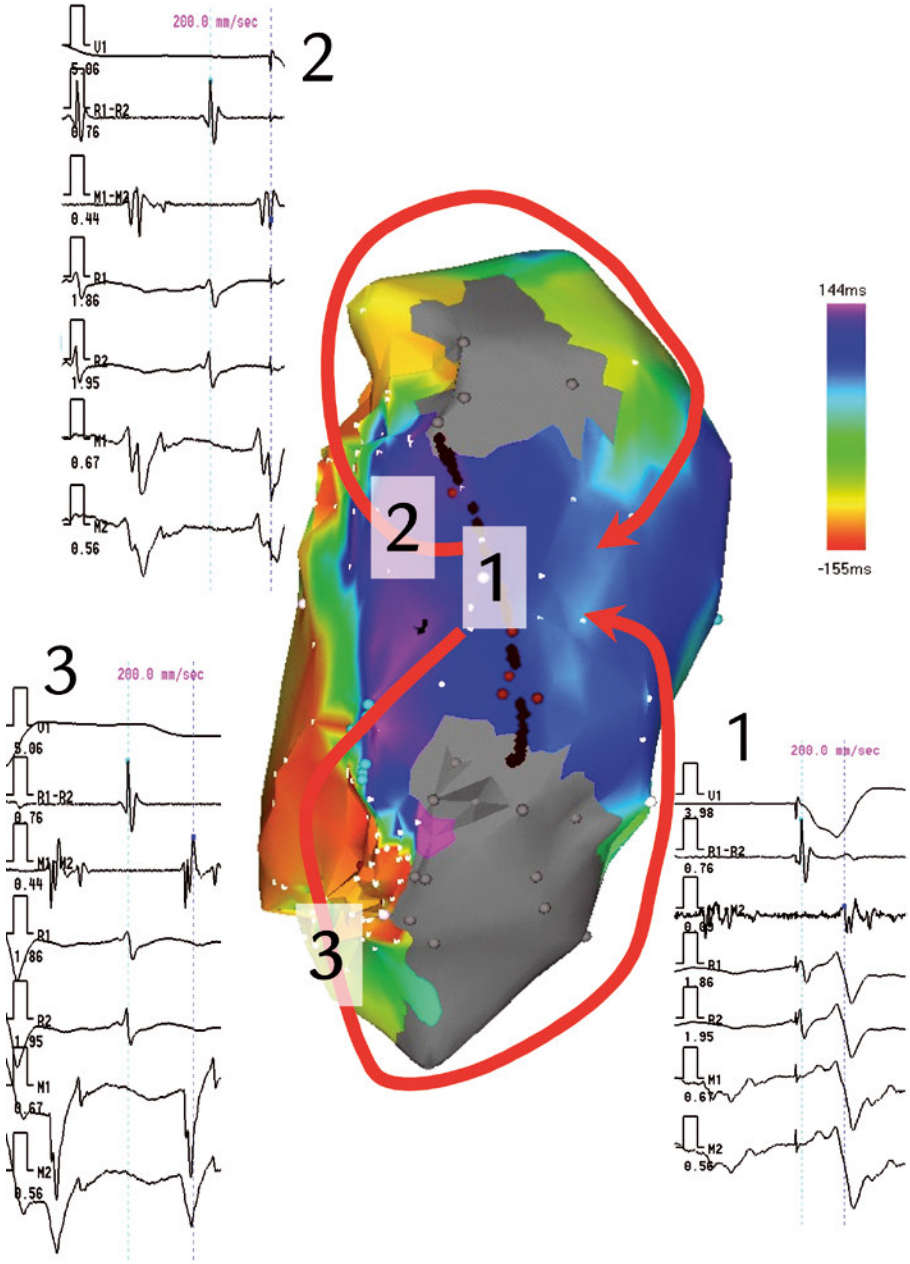

Figure 6.

Color-coded (bipolar) activation map during IART (CL = 290 ms) in patient after Fontan procedure. Two areas of scar tissue (gray zones) were delineated based on 0.1-mV bipolar cutoff value. Tachycardia was caused by figure 8 type reentry (impulse circled around 2 scars as indicated by red arrows). Electrogram panels demonstrate effects of distant electrical activity on both bipolar and unipolar recordings, especially in low-amplitude areas (panel 1). RB indicates bipolar reference; MB, bipolar mapping catheter; RU1, unipolar reference tip; RU2, unipolar reference electrode 2; MU1, unipolar mapping tip; MU2, unipolar mapping electrode 2; bip, bipolar; and uni, unipolar.

In this example (patient after Fontan procedure), the underlying mechanism was a figure of eight type of reentry. In relative normal areas, both unipolar and bipolar recordings can be used to map the spread of activation (panels 2 and 3). However, in the low-amplitude areas (panel 1) far-field signals were present, which made identification of the low-amplitude local unipolar potentials uncertain, whereas the bipolar signals could still be used. RFCA aimed at connecting the two scar areas resulted in termination of the arrhythmia (dotted line).

Outcome of the RF procedure

RFCA was successful (success defined as non-inducibility of the clinical arrhythmia after ablation) in all AVNRT and FAT patients and in 85% and 83% of the IART and AFL patients. Complications were not observed during or after the procedure. During follow-up (18 ± 6 months) only 3 (18%) IART patients and 2 (11%) AFL patients had a recurrence.

Discussion

We demonstrated that significant differences exist between simultaneously recorded unipolar and bipolar signals and consequently between unipolar and bipolar voltage and activation maps in patients with congenital heart disease. These differences not only have impact on the reentrant pathway reconstruction but also on selection of RF target sites.

Unipolar and bipolar electrograms

The shape and amplitude of unipolar and bipolar electrograms and consequently the reconstructed endocardial activation maps are influenced by electrophysiological and structural characteristics of the myocardial tissue involved. Surprisingly, in this era of catheter ablation and detailed endocardial mapping, only few clinical studies addressed the issue of signal morphology and analysis.[7,12-14]

Unipolar recordings offer some advantages compared with bipolar recordings (because they are the subtraction of 2 unipolar signals), for example, unipolar signals may provide essential information about the direction of impulse propagation, which may be helpful in localizing exit points of reentrant circuits and precise localization of accessory pathways, among other things.[26] However, because unipolar recordings are more susceptible to noise and surrounding influences, recording of acceptable unipolar signals is technically challenging.[13,23,24] Additionally, as shown (Figurer 6), unipolar recordings, especially in case of fragmented low amplitude signals may be distorted by far field electrical activity. Bipolar recordings on the other hand are affected by electrode configuration, distance between the recording electrodes, and the direction of the wave front with respect to the electrode orientation. Furthermore, criteria for marking the moment of local activation of complex bipolar electrograms are less well defined.[25] It is therefore not surprising that the reconstruction of endocardial activation patterns depends on the recording technique used and that unipolar and bipolar recordings provide complementary information.

Voltage maps

From computer simulation and experimental studies it is well known that unipolar voltages are larger than bipolar voltages.[13,17] In line with this perception, we demonstrated that unipolar signal amplitudes were higher than the simultaneously recorded bipolar signal in all patient groups.

From the voltage distribution curves a significant difference between patients with and without structural heart disease (e.g. congenital heart disease) could be detected. In patients without structural heart disease the signal amplitudes were significantly larger than those recorded in congenital heart disease patients. The amplitude of an unipolar signal (and consequently the amplitude of the derived bipolar signal) is determined by the volume of the cardiac tissue surrounding the recording electrode activated at the same time. In normal atrial myocardium with intact electrical coupling and normal conduction char-

acteristics, large areas will be activated simultaneously and, the amplitude of the recorded signals will be relatively large. However, if myocardial fibers become separated (e.g. due to aging or in diseased myocardium after surgery), the conduction velocity will decrease and atrial fibers will be activated increasingly a-synchronously.[16,18] In other words, only small areas will be activated at the same time and the amplitude of the recorded signals will decrease. This explains the voltage distribution found in congenital heart disease patients. Surprisingly, a high number of low voltage electrograms were also recorded in AFL patients despite the absence of detectable structural heart disease in the majority of these patients. These findings support observations by others demonstrating increased fragmentation in AFL patients and suggest that, at least in some areas, increased fibrosis resulted in abnormal electrical characteristics.[20-22]

Scar tissue delineation, activation time, and activation maps

Although debate continues about scar tissue cut-off values to be used in congenital heart disease patients, and only limited data are available, we demonstrated that owing to voltage differences between unipolar and bipolar signals it is not justified to use one cut-off value for uni- and bipolar signals because this may have dramatic effects on the reconstructed activation maps.[6,7] Because there is no clear distinction between "normal" and "scar" tissue in patients with and without structural heart disease in the low voltage domain areas, it will not be possible to determine a single unipolar cut-off value. On the other hand, when we studied the bipolar voltage distribution of signals ≤1.0mV it appeared that only in structural heart disease (congenital heart disease) did a significant number of signals have an amplitude of ≤ 0.1mV. Because signals with an amplitude of ≤0.1mV were found in none of the other patient groups, it seems justified to depict 0.1mV as the cut-off value to delineate scar tissue.

Determination of local activation times depends on signal quality and signal characteristics. In case of high amplitude signals, determination of the local activation time is relatively easy. This is supported by our results showing that in patients with normal hearts, automatic marking of both unipolar and bipolar markings required almost no manual adjustments (FAT:98%, AVNRT:95%, AFL:67%) and only minimal differences were detected between unipolar and bipolar activation maps.

However, when low amplitude fragmented signals prevailed (congenital heart disease patients), application of automatic marking algorithms was not possible. From animal studies it is known that the maximum negative derivative of fragmented unipolar electrograms does not always reflect the moment of activation of cells beneath the recording electrode but may reflect activation of bundles at a distance.[14] Hence, assignment of a local activation time to fragmented unipolar– and corresponding bipolar- electrograms is subjected to errors. Moreover, it still unknown which specific component of fragmented bipolar electrograms is related with the local activation time.[25] Given the previous considerations, it is understandable that only minimal differences will be found when comparing unipolar

and bipolar activation maps recorded in patients without structural heart disease. In patients after surgery however, significant differences can be expected.[6,7,9,13]

Clinical implications

Reconstruction of reentrant circuits before ablation depends on meticulous analysis of acquired data. It is therefore not possible to simply state superiority of unipolar or bipolar recordings; the characteristics of both electrode configurations provide complementary information and should be used in combination with voltage and activation mapping. Unipolar recordings provide essential information about the direction of impulse propagation, whereas bipolar signals allow voltage-based scar tissue delineation.

Study limitations

This study is limited by the fact that only 1 specific catheter type and fixed system settings were used. Furthermore, the interoperator/interobserver variability was not studied, which may have affected the manual marking adjustments. Complete right atrial endocardial activation maps were obtained in all patients to assess reliable voltage-distribution curves. Especially in the CHD patients, some overestimation of the number of low-voltage signals may have occurred. This had no effect on the determination of the scar tissue cutoff value, because this value was based on the comparison of voltages found in CHD patients and the other patient groups and not on the frequency distribution. However, we realize that because no sites < 0.1 mV were found in normal hearts, the cutoff value may be a conservative estimate. Furthermore, the cutoff value used to delineate scar tissue is an electrogram definition and is not based on histological studies.

Conclusions

Significant differences exist between simultaneously recorded unipolar and bipolar signals. These differences have considerable impact on reconstruction of complex reentrant pathways and consequently on the outcome of RFCA procedures. In general, unipolar and bipolar recordings provide complementary information; however, only bipolar recordings allow voltage-based scar tissue delineation in CHD patients.

References

1. Lesh MD, Van Hare GF. Status of ablation in patients with atrial tachycardia and flutter. Pacing Clin Electrophysiol. 1994; 17:1026-33.
2. Stevenson WG, Ellison KE, Lefroy DC, Friedman PL. Ablation therapy for cardiac arrhythmias. Am J of Cardiol 1997;80:56-66.
3. Dorostkar PC, Cheng JIE, Scheinman MM. Electroanatomical mapping and ablation of the substrate supporting intraatrial reentrant tachycardia after palliation for complex congenital heart disease. Pacing Clin Electrophysiol 1998;21:1810-1819.
4. Stevenson WG, Delacretaz E, Friedman PL, Ellison KE. Identification and ablation of macroreentrant ventricular tachycardia with the CARTO electroanatomical mapping system. Pacing Clin Electrophysiol. 1998;21:1448-56.
5. Lesh MD, Van Hare GF, Epstein LM, Fitzpatrick AP, Scheinman MM, Lee RJ, Kwasman MA, Grogin HR, Griffin JC. Radiofrequency catheter ablation of atrial arrhythmias. Results and mechanisms. Circulation 1994;89:1074-89.
6. Nakagawa H, Shah N, Matsudaira K, Overholt E, Chandrasekaran K, Beckman KJ, Spector P, Calame JD, Rao A, Hasdemir C, Otomo K, Wang Z, Lazzara R, Jackman WM. Characterization of reentrant circuit in macroreentrant right atrial tachycardia after surgical repair of congenital heart disease: isolated channels between scars allow "focal" ablation. Circulation. 2001;103:699-709.
7. De Groot NMS, Kuijper AFM, Blom NA, Bootsma M, Schalij MJ. 3-D Distribution of bipolar atrial electrogram voltages in patients with congenital heart disease. Pacing Clin Electrophysiol. 2001:24:1334-42.
8. Smeets JLRM, Ben-Haim SA, Rodriguez LM, Timmermans C, Wellens HJJ. New Method for Nonfluoroscopic Endocardial Mapping in Humans: Accuracy Assessment and First Clinical Results. Circulation 1998 97: 2426-2432.
9. Reithmann C, Hoffmann E, Dorwarth U, Remp T, Steinbeck G. Electroanatomical mapping for visualization of atrial activation in patients with incisional atrial tachycardias. Eur Heart J. 2001;22:237-46.
10. Shah DC, Jais P, Haissaguerre M, Chouairi S, Takahashi A, Hocini M, Garrigue S, Clementy J. Three-dimensional mapping of the common atrial flutter circuit in the right atrium. Circulation 1997:96(11):3904-3912.
11. Nakagawa H, Jackman WM. Use of a three-dimensional, nonfluoroscopic mapping system for catheter ablation of typical atrial flutter. Pacing Clin Electrophysiol. 1998 Jun;(6):1279-86.
12. Paul T, Moak JP, Garson A. Epicardial mapping: how to meausure local activation? Pacing Clin Electrophysiol. 1990;13:285-292.
13. Weiss C, Willems S, Rueppel R, Hoffmann M, Meinertz T. Electroanatomical mapping (CARTO™) of ectopic atrial tachycardia: impact of bipolar and unipolar local electrogram annotation for localization the focal origin. J Interv Card Electrophysiol. 2001;5:101-7.
14. Ndrepepa G, Caref EB, Yin H, el-Sherif N, Restivo M. Activation time determination by high-resolution unipolar and bipolar extracellular electrograms in the canine heart. J Cardiovasc Electrophysiol. 1995;6:174-88.
15. Callans DJ, Ren JF, Michele J, Marchlinski FE, Dillon SM. Electroanatomic left ventricular mapping in the porcine model of healed anterior myocardial infarction. Correlation with intracardiac echocardiography and pathological analysis. Circulation 1999; 100:1744-1750.
16. Spach MS, Dolber PC. Relating extracellular potentials and their derivatives to anisotropic propagation at a microscopic level in human cardiac muscle. Evidence for electrical uncoupling of side to side fiber connections with increasing age. Circ Res 1986;58:356-371.
17. Gallagher JJ, Kasell JH, Cox JL, Smith WM, Ideker RE, Smith WM. Techniques of intraoperative electrophysiologic mapping. Am J Cardiol 1982;49(1):221-240.
18. Roberts DE, Scher AM. Effect of tissue anisotropy on extracellular potential fields in canine myocardium in situ. Circ Res 1982;50:342-351.
19. de Groot N, Bootsma M, van der Velde ET, Schalij MJ. Three-dimensional catheter positioning during radiofrequency ablation in patients: first application of a real-time position management. JCE 2000;11:1183-1192.

20. Watson RM, Josephson ME. Atrial flutter 1. Electrophysiologic substrates and modes of initiation and termination. Am J Cardiol 1980:45;732-739.
21. Cosio FG, Arribas F, Palacios J, Tascon J, Lopez-Gil M. Fragmented electrograms and continuous electrical activity in atrial flutter. Am J Cardiol 1986;57:122-130.
22. Tanigawa M, Fukatani M, Konoe A, Isomoto S, Kadena M, Hashiba K. Prolonged and fractionated right atrial electrograms during sinus rhythm in patients with paroxysmal atrial fibrillation and sick sinus node syndrome. J Am Coll Cardiol 1991;17:403-8.
23. Blanchard SM, Damiano RJ, Asano T, Smith WM, Ideker RE, Lowe JE. The effects of distant electrical events on global activation in unipolar epicardial electrograms. IEEE Trans Biomed Engineering 1987;34:539-546.
24. Bakker JMT, Hauer RNW, Simmers TA. Activation time mapping: unipolar versus bipolar recording. In: Cardiac electrophysiology from cell to bedside. Eds. D.Zipes&P.Jalife. Philadelphia: WB Saunders Company, 1995: 1068-1078.
25. Biermann M, Sheanasa M., Borggrefe M, Hindricks G, Haverkamp W, Breithardt G. The interpretation of cardiac electrograms. Eds. M Sheanasa, Borggrefe M, G. Breithardt. In: Cardiac Mapping. New York, Futura Publishing:1993 ;11-34.