

# Non-Invasive Estimation Of Left Atrial Dominant Frequency In Atrial Fibrillation From Different Electrode Sites: Insight From Body Surface Potential Mapping

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## Abstract

The dominant driving sources of atrial fibrillation are often found in the left atrium, but the expression of left atrial activation on the body surface is poorly understood. Using body surface potential mapping and simultaneous invasive measurements of left atrial activation our aim was to describe the expression of the left atrial dominant fibrillation frequency across the body surface.

20 patients in atrial fibrillation were studied. The spatial distributions of the dominant atrial fibrillation frequency across anterior and posterior sites on the body surface were quantified. Their relationship with invasive left atrial dominant fibrillation frequency was assessed by linear regression analysis, and the coefficient of determination was calculated for each body surface site.

The correlation between intracardiac and body surface dominant frequency was significantly higher with posterior compared with anterior sites (coefficient of determination  $67 \pm 8\%$  vs  $48 \pm 2\%$ ,  $p < 0.001$ ). The site with largest coefficient of determination was 79.6% ( $p < 0.001$ ) and was a posterior site. In comparison with the site closest to lead V1 it had a coefficient of determination of 23.0% ( $p = 0.033$ ), and with the posterior body surface site closest to lead V9 had a coefficient of determination of 70.3% ( $p < 0.001$ ).

Left atrial dominant fibrillation frequency was more closely represented at posterior body surface sites.

## Introduction

Atrial fibrillation (AF) is distinguished by fast and irregular electrical activity of the atria. The prevalence of AF in the developed world is approximately 2% of the general population, with the average age of 75 years.<sup>1</sup> Un-medicated patients in AF have a much higher risk of stroke and AF may be a common etiological factor for one quarter of strokes with unknown cause.<sup>2</sup> Ablation has become a common treatment option for AF with the aim of restoring sinus rhythm by targeting atrial high dominant frequency (DF) fibrillation foci or drivers of AF. Clinical assessment of atrial DF foci is based on invasive electrophysiological (EP) studies. Such studies typically take

several hours and it would be highly desirable to have a preliminary assessment of atrial DF drivers non-invasively prior to undertaking the invasive procedure. Several studies have shown that there is strong correlation between invasively measured intracardiac activation rates and DF measured from the body surface ECG.<sup>3</sup> Typically, lead V1 has been used for this assessment since it exhibits a high amplitude atrial signal compared to other ECG leads.<sup>4</sup> However, the 12-lead ECG is not specifically designed to record atrial activity prompting a number of studies to assess more optimal lead configurations.<sup>5</sup> Nor is it well understood how electrical activity from the LA contributes to the ECG. This is important since the high frequency drivers of the arrhythmia are predominantly found in the left atrium (LA).<sup>6</sup> Studies have shown that additional information about the atrial activity can be obtained from adaptation of the 12-lead ECG by additional leads on the back (V7, V8 and V9).<sup>5,7,8</sup> A technique using many additional leads to the 12-lead ECG known as body surface potential mapping (BSPM) allows greater spatial coverage of the torso for investigating optimal sites for observing atrial activity.<sup>9,10</sup> The aim of this study was to investigate the spatial distribution of dominant atrial fibrillation frequency using body surface potential mapping and to determine the sites with dominant frequencies which are representative of the invasively recorded left atrial electrogram (EGM) dominant

## Key Words:

Atrial Arrhythmia, Atrial Fibrillation, Intra-Atrial Electrograms, Body Surface Potential Mapping, Signal Processing.

Disclosures:  
None.

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**Table 1:** Patient characteristics

Subject	Gender		Age (year)	BMI (kg/m <sup>2</sup> )	AF classification	
	Male	Female			Paroxysmal	Persistent
1	✓		55	26.3		✓
2	✓		69	25.9	✓	
3	✓		61	24.0	✓	
4	✓		68	27.7	✓	
5	✓		72	28.1		✓
6		✓	66	25.0		✓
7		✓	61	38.5		✓
8	✓		68	33.3	✓	
9	✓		56	24.3	✓	
10	✓		56	26.3	✓	
11	✓		52	33.7		✓
12	✓		40	26.2	✓	
13	✓		64	28.4		✓
14	✓		61	26.3	✓	
15	✓		59	27.2	✓	
16		✓	71	39.0		✓
17	✓		63	34.8	✓	
18	✓		70	30.9	✓	
19	✓		47	27.9	✓	
20	✓		49	26.2	✓	

frequencies.

## Methods

### Study Group

20 patients admitted for AF catheter ablation to Freeman Hospital were analysed. Ethical approval for the study was granted and informed consent was obtained from all patients. There were 7 cases of persistent AF and 13 cases of paroxysmal AF. Subjects were predominantly male (17 male vs 3 female) and had a mean (sd) age of 60 (9) years and body mass index of 29 (5) kg/m<sup>2</sup>. Table 1 provides the individual patient characteristics.

### Data Recordings

Two minute recordings of the heart electrical activity were obtained simultaneously from BSPM and intracardiac catheterisation in the EP lab prior to the ablation procedure. BSPM comprised 64 monopolar leads and 3 bipolar limb leads acquired using the BioSemi ActiveTwo™ recording system (BioSemi, Amsterdam, Netherlands). The spatial arrangement of the body surface electrodes is illustrated

in Figure 1.

Intracardiac recordings comprised 5 bipolar signals acquired by a decapolar pulmonary vein ablation catheter (PVAC) (Ablation Frontiers, CA, USA) and recorded on a Bard EP system (Figure 1). The catheter was positioned inside the LA against one of the pulmonary veins.

### Body Surface Dominant Frequency

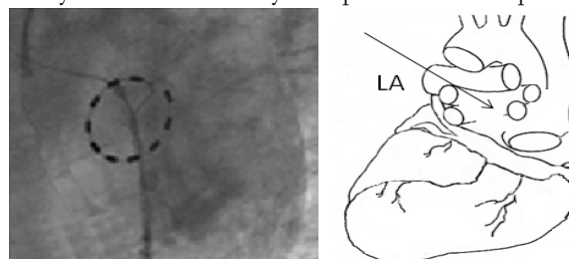
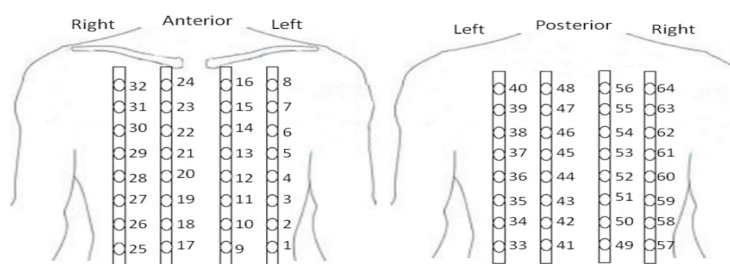
The DF of BSPM recordings was derived according to a previously published procedure.<sup>11,12,13</sup> Specifically, the BSPM recordings were down-sampled from the original sample rate of 2048 Hz to 512 Hz. This allowed reduction of computation time and memory requirement without loss of atrial spectral information since AF exhibits DF in the low frequency range, typically 3-9 Hz.<sup>14</sup> The Wilson Central Terminal was computed and subtracted from the signals recorded at the 64 body surface sites to obtain 64 precordial leads. Baseline wander and high frequency noise were removed using a band-pass filter with bandwidth of 0.5 to 100 Hz (second order, infinite impulse response (IIR), elliptical filter). Automatic ventricular beat detection was carried out by means of a threshold-based QRS detector and all detected beats confirmed by visual inspection. Averaged-QRST template beat subtraction with morphology clustering was used to suppress the ventricular activity, leaving the residual AF signal for further analysis.<sup>13</sup> Power spectral density (PSD) of the AF signal was computed with a resolution of 0.125 Hz using the Welch periodogram with a sliding Hamming window of 8 seconds and a 1 second overlap. DF was calculated for each BSPM site as the PSD frequency component with the highest power in the AF frequency range of 3-9 Hz.

### Intracardiac Dominant Frequency

DF of the LA recordings was derived using the technique of Botteron and Smith.<sup>15,16</sup> Specifically, the bipolar recordings were down-sampled from the original sample rate of 1000 Hz to 512 Hz in accordance with the BSPMs. They were then band-pass filtered (40-250 Hz, second order, IIR, Butterworth) and any far-field ventricular activity cancelled. Following rectification and further low-pass filtering (20 Hz), PSD and DF were calculated in the same manner as for the BSPM recordings.

### Data Analysis

Colour maps of body surface DF were plotted for each subject from which the structure of the spatial variation in body surface DF could be observed. Spatial variability in body surface DF was also quantified by statistical summary data presented as boxplots.

**Figure 1:**

**Illustration of 64-lead BSPM positions on the body surface (top), and PVAC inside the LA (bottom). The 64 leads from the body surface were arranged in 8 flexible rubber strips (length of 33 cm), with 8 electrodes on each strip (each 45 mm apart), 4 strips located on the anterior torso (32 anterior electrodes), and 4 strips located on the posterior torso (32 posterior electrodes). The intracardiac catheter was a 10-electrode catheter with 3 mm long electrodes and 3 mm spacing between each electrode (bottom left) and positioned within the left atrium (bottom right). Intracardiac bipolar signals were derived from each adjacent pair (5 pairs) of electrodes.**

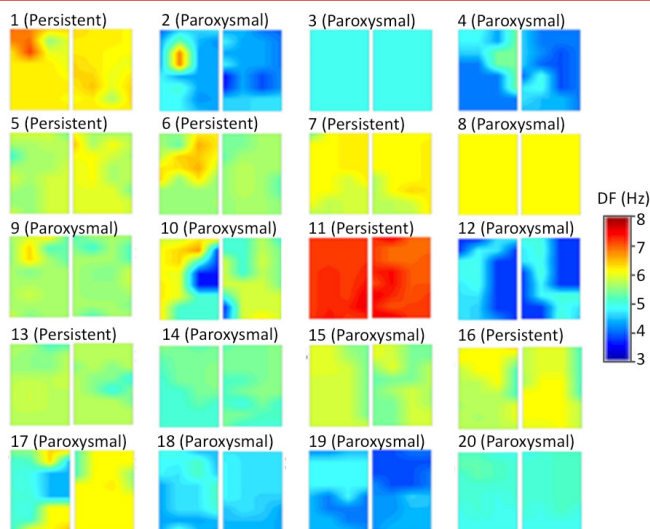


Figure 2:

**Spatial distribution of dominant frequencies from the body surface for each subject (identified as 1 to 20). Colours represent dominant frequencies and the maps are in accordance with the electrode positions illustrated in Figure 1 with the anterior sites shown on the left and posterior sites on the right for each subject. The clinical AF classification for each patient is shown adjacent to the subject number.**

The variability in DF across the 5 LA intracardiac bipoles was quantified by statistical summary data presented as boxplots.

Statistical differences of DF between subjects were assessed by the Friedman test for related samples.

Using DF measurements for all subjects the linear correlation between median LA DF (i.e. invasively measured DF) and DF at each body surface site was calculated using regression analysis and the agreement quantified by coefficient of determination ( $R^2$ ).

To compare specific anterior and posterior body surface positions, sites 22 and 46 were chosen. Site 22 was the closest to lead V1 electrode position which is commonly used for analysis of AF on account of its high amplitude atrial signal. Site 46 was the closest to lead V9 electrode position, which has been suggested as a lead with good representation of the LA activity.<sup>5,7,8</sup> For all tests the null hypothesis was rejected if the p-value was less than the significance level of 0.05.

## Results

### Body Surface Spatial Distribution Of DF And Its Variability Between Subjects

The majority of subjects exhibited spatial variability of DF across the body surface as illustrated in Figure 2. However, two subjects had a constant DF across all body surface sites (subjects 3 and 8), although they did not have the same DF.

As expected there was a significant difference in body surface DF between subjects with subject median values ranging from 4.2 Hz (subject 12) to 7.5 Hz (subject 11) ( $p < 0.001$ , Friedman test). Similarly, from the intracardiac recordings, the LA DF showed a significant difference between subjects with median values ranging from 4.4 Hz (subject 19) to 7.2 Hz (subject 7) ( $p < 0.001$ , Friedman test).

For each subject considering the median DF across sites, the DFs were significantly higher for persistent AF compared to paroxysmal AF cases for both body surface (mean (sd) 6.4 (0.5) Hz vs 5.4 (0.9) Hz,  $p = 0.02$ ) and intracardiac recordings (6.1 (0.7) Hz vs 5.3 (0.7) Hz,  $p = 0.03$ ).

We assessed the temporal stability of the recordings by analysing the differences in median DFs across sites between the first and second minute of the recordings for which no significant differences were found for either body surface (median (IQR) minute 1: 5.75 (4.8 - 6.4) Hz vs minute 2: 5.8 (4.9 - 6.1) Hz) or intracardiac (minute 1: 5.9 (4.9 - 6.2) Hz vs minute 2: 5.6 (5.1 - 6.1) Hz) recordings.

### Relationship Between Body Surface And Left Atrial Dominant Frequencies

Figure 3 compares the DF from body surface and left atrial sites. The median values agreed within 1 Hz but there were large differences when considering individual leads. For example, for subject 10, although median body surface and LA DF agreed within 0.07 Hz, differences in DF in some individual leads from median LA DF were more than 2 Hz. The DF map for this subject (Figure 2) showed a large area of low DF in the left anterior sites, much lower than median LA DF of 6 Hz. Note that for the subjects with no spatial variation in DF (subjects 3 and 8), there was no difference between the body surface and LA DF.

Figure 4 shows the regression plots for the anterior site 22 (equivalent to V1) and the posterior site 46 (equivalent to V9). V1 had  $R^2 = 23.0\%$ ,  $p = 0.033$  and V9 had  $R^2 = 70.3\%$ ,  $p < 0.001$ . The distribution of  $R^2$  across the body surface is illustrated in Figure 5.  $R^2$  was significantly higher on posterior compared with anterior sites ( $67 \pm 8\%$  vs  $48 \pm 2\%$ ,  $p < 0.001$ ). The greatest correlation across all sites was at posterior site 59 ( $R^2 = 79.6\%$ ,  $p < 0.001$ ). Site 16 had the highest correlation of the anterior sites ( $R^2 = 68.1\%$ ,  $p < 0.001$ ).

## Discussion

It has previously been shown that frequency analysis of the surface ECG may prove useful for non-invasive assessment of the electrophysiological state of the atria in patients with AF.<sup>9,14</sup> In this study the linear relationship between left atrial activations and body surface DF was investigated using BSPM. This has not previously been studied. Previous works have carried out similar studies, but they have been performed with different body surface resolution or to explore different sources of atrial activations. For example, in a study on 14 patients it was observed that body surface DFs were localised to the nearest atrium and were able to capture the regional differences in atrial activation rates.<sup>9</sup> Also, it has been shown that there is good correlation between body surface and invasive atrial activity in AF

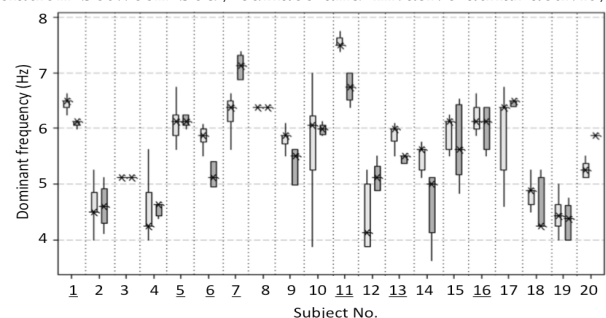


Figure 3:

**Dominant frequencies of body surface (light gray) and left atrium (dark gray) sites for each subject. Asterisks give the median across all recording sites (64 body surface sites, 5 pairs of left atrial sites) for each subject. The box is the inter-quartile range (IQR), and whiskers extend to the smallest and largest non-outliers. Not shown are outlying values which are dominant frequencies 1.5 x IQR above (below) the upper quartile (lower quartile). Subject numbers of persistent AF cases are underlined.**



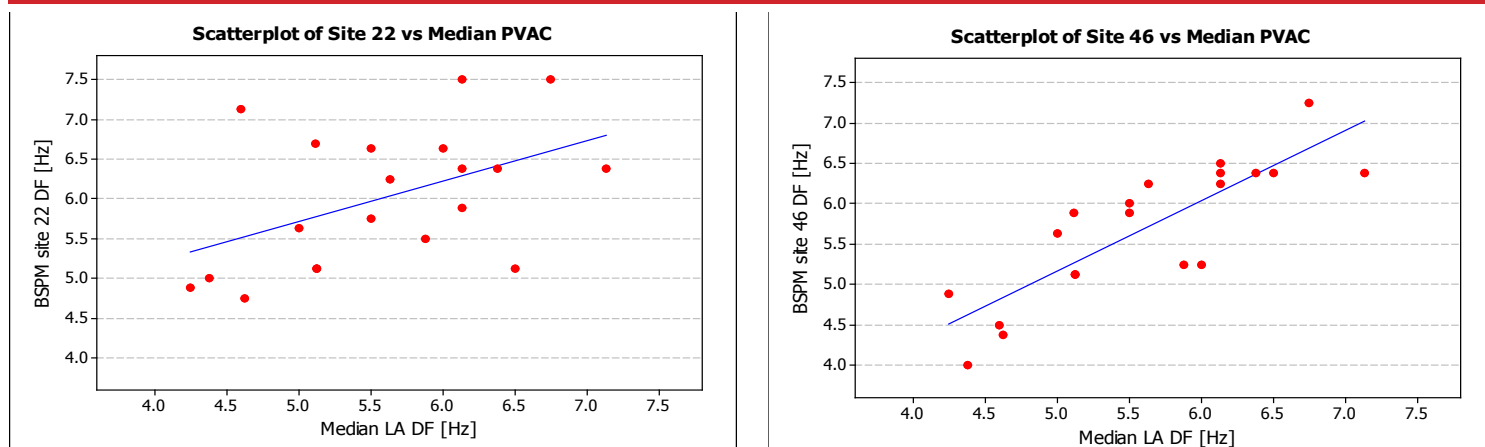


Figure 4:

Linear regression of median left atrium dominant frequency and anterior site 22 (equivalent to lead V1) (top,  $R^2 = 23.0\%$ ), and posterior site 46 (equivalent to lead V9) (bottom,  $R^2 = 70.3\%$ ). There are 19 points visible as subjects 3 and 12 had overlapping values of DF.

such that the fibrillatory activity observed in ECG lead V1 correlated primarily with the activity of the right atrium (RA).<sup>17</sup> In a similar way, DF from the RA and coronary sinus recordings has been quantified with the values obtained from three surface leads, such as aVF, V1 and V5.<sup>14</sup> These studies have been facilitated by algorithmic developments, such as the study by Holm et al, which allow the atrial component of the ECG to be exploited.<sup>18</sup> Studies have measured the correlation between DF obtained from non-contact endocardial signals of the RA with lead V1.<sup>19</sup> Likewise, intracardiac mapping of DF has been performed to study the influence of atrial sites on the surface ECG leads.<sup>17,20</sup> By comparing DF extracted from the 64-lead BSPM with simultaneous invasive measurements of the LA activations, our study showed that the LA DF is best characterised on the posterior body surface. This agrees with previous studies which have suggested posterior lead positions such as V9 are representative of the LA activity.<sup>7,9,10,11</sup> DFs from V9 showed better agreement with those of LA than for lead V1 which is commonly used for assessment of AF.

Despite the clinical classification of AF in all the subjects, at the time of recording two of the subjects in our study exhibited a single DF across all body surface sites which were in agreement with the invasively recorded LA DF. This is consistent with a model of AF in these patients of a single, highly stable re-entrant circuit or trigger. So, as would be expected, a single AF source would be the dominant feature at all body surface sites. All other subjects exhibited some degree of variation of DF across the body surface and we have shown that the posterior sites were most representative of the invasively recorded LA DFs. The body surface pattern of AF DF in these subjects likely represents the complex underlying activation patterns of multiple re-entrant circuits or triggers in these patients.

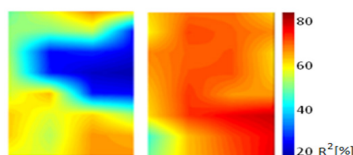


Figure 5:

Linear regression of body surface and LA median DF displayed as a spatial map to identify spatial differences in  $R^2$ . Colours represent the correlation values. Posterior sites (right panel) exhibited the highest correlations with  $R^2$  values of up to almost 80%.

It should be noted that the study has several limitations. Particularly, although comparable to other studies, a relatively small number of patients were studied. This precluded an analysis of the correlation between body surface and intracardiac DF for subgroups of persistent and paroxysmal AF cases. Moreover, relatively small numbers of recording sites in the left atrium have been used to represent the left atrial activations. Extensive invasive mapping studies were not available, nor were invasive recordings in the RA available. Consequently, it was not possible to relate right atrial activations to the body surface recordings. However, this study was not designed to identify the driving source for AF in the individual patient.

### Conclusion:

Left atrial dominant fibrillation frequency is more closely represented by the dominant frequencies at posterior body surface sites.

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