Localizing the Accessory Pathway in Ventricular Preexcitation Patients Using a Score Based Algorithm

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Accessory pathway, algorithms, delta wave, electrocardiography, Wolff-Parkinson-White syndrome

Summary
Objectives: Clinical data was analyzed to find an efficient way to localize the accessory pathway in patients with ventricular preexcitation.
Methods: The delta wave morphologies and ablation sites of 186 patients who underwent catheter ablation were analyzed and an algorithm (“locAP”) to localize the accessory pathway was developed from the 84 data sets with a PQ interval ≤0.12 s and a QRS width ≥0.12 s. Fifty additional patients were included for a prospective validation. The locAP algorithm ranks 13 locations according to the likelihood that the accessory pathway is localized there. The algorithm is based on the locAP score which uses the standardized residuals of the available data sets.
Results: The locAP algorithm’s accuracy is 0.54 for 13 locations, with a sensitivity of 0.84, a specificity of 0.97, and a positive likelihood ratio of 24.94. If the two most likely locations are regarded, the accuracy rises to 0.79, for the three most likely locations combined the accuracy is 0.82. This new algorithm performs better than Milstein’s, Fitzpatrick’s, and Arruda’s algorithm both in the original study population as well as in a prospective study.
Conclusions: The locAP algorithm is a valid and valuable tool for clinical practice in a cardiac electrophysiology laboratory. It could be shown that use of the locAP algorithm is favorable over the localizing algorithms that are in clinical use today.

1. Introduction

1.1 Clinical Importance

Ventricular preexcitation, or the Wolff-Parkinson-White (WPW) electrocardiogram (ECG) abnormality, occurs when the atrial impulse activates the ventricles prematurely due to abnormal muscular connections called accessory atrioventricular (AV) pathways. Tachyarrhythmias can occur as a result of the accessory pathway [1]. The classic WPW syndrome results from a pathway that is capable of bidirectional conduction. The prevalence of the WPW syndrome is estimated to be 0.1–0.3%, with boys being affected twice as common. The age distribution shows peaks during the first year and early childhood [1, 2]. The most serious complication of WPW syndrome is sudden cardiac death (SCD).

WPW syndrome can be treated using catheter ablation (i.e., radiofrequency or cryoablation) of the AV accessory pathway [3–5], but also using surgical ablation techniques or pharmacological therapy [1]. Current clinical guidelines suggest catheter ablation for symptomatic forms of the WPW syndrome [6–8] but not for asymptomatic forms [6].

1.2 Ventricular Preexcitation and the Electrocardiogram

The definition of WPW syndrome relies on the following electrocardiographic features [5, 9]:
1. A PQ interval ≤0.12 s,
2. with a slurring and slow rising of the initial segment of the QRS complex, known as a delta wave,
3. a widened QRS complex with a total duration ≥0.12 s, and
4. secondary repolarization changes reflected in ST segment-T wave alterations that are generally directed opposite to the major delta wave and QRS complex.

However, there are variable electrocardiographic manifestations of accessory pathways. The degree of preexcitation depends on the relative contributions of accessory pathway conduction and conduction over the specialized conduction system to ventricular depolarization [2].
The delta wave, defined as a slurring and slow rising of the initial segment of the QRS complex, results from anterograde conduction over the accessory pathway. If a delta wave is present, it can have positive (Fig. 1a), negative (Fig. 1b), or biphasic morphology (Fig. 1c).

1.3 Algorithms to Localize the Accessory Pathway

Localization of the AV accessory pathway is important for a successful and efficient catheter ablation procedure. An ablation site on the right free wall is generally associated with less risk than a left free wall ablation site, as the catheter is usually inserted into the heart chambers through the venous system. A septal ablation site can result in an increased rate of complications because of the possibility of ablating the AV conduction system. Still, the final localization of the accessory pathway remains to be determined invasively and is defined as the site of successful catheter ablation.

The surface ECG can provide important information regarding the approximate location of the accessory pathway. Anterograde conduction over the pathway causes premature activation of the ventricles at the ventricular insertion site of the accessory pathway. The vector of initial ventricular depolarization is reflected by the delta wave morphology. The main component of the QRS complex represents the relative contributions of the accessory pathway and the specialized AV conduction system. Various ECG algorithms to localize the site of the accessory pathway have been described. These algorithms are based on delta wave morphology, QRS morphology, or both [10–12]. However, the ability of a twelve lead ECG to resolve the precise location of the accessory pathway is limited. The orientation of the heart in the chest cavity is the main contributor to the ECG morphology, while the site of the accessory pathway on the AV annulus has limited influence on the surface ECG vector. The degree of preexcitation, the coexistence of other ECG abnormalities, and the presence of multiple accessory pathways are also important factors that influence accurate localization [2].

All known existing algorithms to detect the location of the accessory pathway follow a tree based approach, i.e., the attending physician has to make some binary decisions in order to identify the algorithm’s result [10–14]. These algorithms have their limitations in a clinical setting, as they are potentially complicated and time consuming to apply and as they only provide a very limited number of distinct locations (e.g., as low as four for Milstein’s algorithm and up to ten for Arruda’s algorithm).

2. Objectives

The existing algorithms provide room for improvement due to issues described above. Therefore, the objective of this study was to analyze available clinical data and to find an efficient and accurate way to determine the location of the accessory pathway in patients suffering from ventricular preexcitation, based solely on the morphology of the delta waves.

3. Methods

3.1 Participants

Between 1997 and 2007, 186 patients with WPW syndrome who underwent successful catheter ablation in the catheter laboratory of the Division of Cardiology (Department of Internal Medicine, Medical University Innsbruck) in Innsbruck, Austria were included. Written informed consent for the catheter ablation procedure was obtained from all patients. The locations of the accessory pathway and the delta wave morphologies (Fig. 1) of these patients were used for this study. The location of the accessory pathway was defined as the site of successful catheter ablation. The location was verified using radiologic findings. No multiple accessory pathways could be ob-

![Fig. 1](image) The delta wave morphology in an ECG (a … positive; b … negative; c … biphasic). The black calipers mark the onset and end of the delta wave, the gray area marks the area/integral beneath the delta wave.
observed. The morphology of the delta wave was determined within the initial 100 ms of the preexcitation, which is similar to the definition of the delta wave used by Arruda et al. [10]. Each patient’s delta wave morphologies were determined for the twelve leads of the clinical standard ECG by three independent experts (MCS, KS and KE). Classifications where the findings of these three experts were not in agreement were set to “unknown”. The mean age at ablation was 35 ± 14 years (minimum 8, maximum 66). The study population included 20 patients below the age of 18.

Only 84 patients had a QRS width ≥0.12 s and a PQ interval ≤0.12 s. Following the clinical definition of the WPW ECG pattern, only those 84 data sets were used for algorithm development. Of these 84 patients, twelve were below the age of 18 at the time of ablation.

Fifty adult patients (mean age 36 ± 13 years) with single accessory pathways who were successfully ablated between 2008 and 2011 formed the study population for the algorithm development. Of these 84 patients, twelve were below the age of 18 at the time of ablation.

3.2 Analysis of the Data

The ablation site was classified as one of the 13 distinct locations provided by the clinical standard nomenclature and the anatomically correct nomenclature [15]. The abbreviations for the locations used in this report are shown in Table 1. The different nomenclatures are shown schematically in a left anterior oblique (LAO) view of the AV annuli in Figure 2. Note that using these 13 locations follows an electrophysiology consensus statement on the localization of accessory pathways [15], in contrast to the different localization schemes – with generally fewer distinct locations – used by the current algorithms in place that were introduced in Section 1.3. Note also that there are no left septal locations defined because cardiac electrophysiologists generally ablate all septal pathways from the right side, if possible. The clinical standard nomenclature and the anatomically correct nomenclature are interchangeable. As the clinical standard nomenclature is still more widely used, this nomenclature was used in this text.

The frequency (the number of observed cases) of every location is shown in Table 2. The data sets were analyzed statistically using a cross table for every ECG lead. In each cross table the delta wave morphologies were placed in the columns and the locations were placed in the rows. An example of such a cross table (for lead V1) is shown in Table 3. As can be seen from Table 3, negative delta waves in lead V1 seem to be associated with right or septal accessory pathways, whereas positive delta waves are associated with left pathways.

The observed frequency, the expected frequency and the standardized residual were calculated for each cell of these cross tables. The expected frequency is

$$\sum o_i \times \sum o_j \over N$$

where \(\sum o_i\) is the sum of observed frequencies in the \(i\)-th row, \(\sum o_j\) is the sum of observed frequencies in the \(j\)-th column, and \(N\) is the overall number of observations. The standardized residual is defined as the square root of the Chi squared value \(X^2\), where \(X^2 = \sum (o_i - e_i)^2 \over e_i\), where \(o_i\) is the observed frequency and \(e_i\) is the expected frequency for the cell in the \(i\)-th row and the \(j\)-th column. Note that the sum of all differences \(o_i - e_i\) is 0 because the observed and expected frequencies add up to the same sample size \(N\) [16]. Thus, the standardized residual is defined as

$$X_i = \sqrt{\frac{o_i - e_i}{e_i}}$$

Note that \(X_i\) has approximately a standard normal distribution [16]. A positive standardized residual means that the observed frequency is higher than the expected frequency, whereas a negative standardized residual means the opposite. Standardized residuals are suited very well for the given purpose as they provide a reliable measure for the likeliness that a given delta wave morphology corresponds to a certain location. Especially, this measure is not biased by the frequency of a certain location in the data (Table 2), as would be the case for “normal” residuals \(o_i - e_i\). The tables with the standardized residuals were the data base for the developed algorithm.

3.3 Development of the locAP Algorithm

It was investigated whether a more quantitative approach than the standard tree based approach was feasible and favorable. Thus, a score based algorithm was developed. The statistical criteria outlined above.

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were used. This algorithm was called “locAP” and is based on the “locAP score”. The locAP score was computed by summing up the standardized residuals of the given delta wave morphologies; this was done for all locations. The location with the highest score was considered to be the most likely position of the accessory pathway. Equal scores were sorted according to their frequency in the data set (Table 2).

Figure 3 shows a sample ECG, the corresponding delta wave classifications, the locAP scores, and the correct prediction of the location of the accessory pathway.

The computation of the locAP scores has complexity $O(L \times M)$, where $L$ is the number of leads (12) and $M$ is the number of locations (13). Hence, a constant number of $12 \times 13 = 156$ operations is needed. The complexity of sorting the locAP scores depends on the sorting algorithm that is used. For example, the sorting algorithm “Quicksort” has a worst case complexity of $O(M \log M)$ (169 operations). As all variables that contribute to the complexity are known constants, the overall complexity of the locAP algorithm can be considered $O(C)$, where $C$ denotes a constant. Therefore, computation of the locAP score is computationally efficient.

### 3.4 Comparison of Algorithms

The locAP algorithm still had to be compared with other algorithms that are currently in use in clinical practice. Hence, a clinical expert (MCS) applied Milstein’s [12], Fitzpatrick’s [11] and Arruda’s [10] algorithms blindly (he did not know the actual ablation site) to the available data. The accuracies of these algorithms were then compared to the accuracy of the locAP algorithm. The accuracy was defined as the ratio of correct classifications to all data sets.

As these algorithms use different localizing patterns and, also, a different number of distinct locations, only pairwise comparisons between the locAP algorithm and the other algorithms were made. For each comparison, some clinical standard locations were grouped together. A result was defined as correct if the location as determined by the algorithm lay in the same grouping of locations as the actual ablation site.

### 3.5 Statistical Methods

Where applicable, the structure of this study report was based on the structure suggested by the STARD (Standards for Reporting of Diagnostic Accuracy) initiative [17, 18]. In addition to the accuracy, we determined sensitivity, specificity, positive predictive value, 95% confidence intervals, and the positive likelihood ratio. An unpaired t test was used to compare the means of the locAP scores for correct and incorrect classifications. A p value $\leq 0.05$ was considered significant.

Note that a “diagnostic test” in this study refers to the locAP algorithm and that a “disease” or “condition” refers to the ablation site. These figures were calculated for each of the 13 locations, the weighted averages of these 13 location values were used for the overall numbers [10]. Sensitivity and positive predictive value were weighted by the number of true positives, specificity was weighted by the number of true negatives.

### 3.6 Software Environment

MATLAB (The MathWorks, Inc., Natick, MA, USA) was used for developing and validating the algorithms as it allows for fast and flexible testing and adaptation of algorithms. Statistical analyses were performed using SPSS, R, and Microsoft Excel. Software applications (see Sec. 5.1) using
the locAP algorithm were written using the Java and C++ programming languages.

4. Results

4.1 The locAP Algorithm’s Accuracy

The locAP algorithm was accurate in 54% of the cases for valid data sets. A result was defined as correct if the location with the highest score matched the ablation site as determined by the radiologic findings. The accuracy was defined as the ratio of correct classifications to all data sets. Besides computing a most likely location, the locAP algorithm also provides a second most likely location and so forth. If also the second most likely location was included, the accuracy rose from 0.54 to 0.79 (i.e., the ablation site was identical to either the most likely or the second most likely location as determined by the locAP algorithm in 79% of cases). If also the third most likely location was included, the accuracy was 0.82. Furthermore, the most likely location lay at or next to the location of the ablation site in 71% of cases. Such a neighborhood was defined as two locations lying next to each other on the same AV annulus.

The locAP algorithm was then also tested on all 186 data sets, including those data sets with a QRS width <0.12 s and with a PQ interval >0.12 s. Note that the locAP algorithm was developed using only 84 of these data sets, so the other 102 data sets did in no way influence the calculation of the standardized residuals and were so to speak “unknown” to the algorithm. For all 186 data sets, the accuracy of locAP was 0.53. If the second most likely location was included, the accuracy was 0.74, if also the third most likely location was considered, the accuracy was 0.78. In 69% of cases the most likely localization was in the direct neighborhood of the ablation site.

When the pediatric study population (age at ablation <18) of the valid data sets was considered by itself (n = 12), the accuracy was 42%. If also the second-highest locAP score was considered, the accuracy rose to 75%. For the 20 patients below the age of 18 in the entire study population, the accuracy was 55%. The accuracy in this population was 75% if also the second-highest locAP score was taken into account.

![Fig. 3](image-url)

**Fig. 3** A representative example of a patient with an accessory pathway for whom the locAP algorithm was applied and where the location of the accessory pathway was predicted correctly at a posteroseptal (PS) site. a) The patient’s ECG. b) The delta wave morphologies. c) The computed locAP scores. d) The 13 locations and the likelihood that the accessory pathway lies there (1. … most likely location, 13. … least likely location).
The locAP algorithm’s accuracy was compared with the accuracies of Milstein’s [12], Fitzpatrick’s [11] and Arruda’s [10] algorithms as defined in Section 3.4. The accuracies are shown in Table 4 for the valid data sets and in Table 5 for all 186 data sets. Table 6 shows the comparisons for the 50 data sets of the prospective study population. The locAP algorithm achieved the highest accuracies in all comparisons, thus validating locAP both retro- and prospectively.

### 4.3 Statistical Results

The mean locAP score of all first ranked locations was $9.84 \pm 4.80$ (min 2.28, max 22.63). The mean locAP score of the correct localizations was $11.51 \pm 5.27$ (min 2.28, max 22.63), the mean score of the incorrect localizations was $7.92 \pm 3.33$ (min 2.37, max 17.12; $p = 0.0004$), showing that correct localizations received higher locAP scores.

A cross table with the observed frequencies of the locations classified by the locAP algorithm and the ablation sites is shown in Table 7. The statistical values (see Sec. 3.5) shown in Table 8 were calculated with these frequencies. Overall sensitivity was 84% (95% confidence interval: 76%–92%), specificity was 97% (95% confidence interval: 96%–98%), the positive predictive value was 61%, and the positive likelihood ratio was 24.94.

### 5. Discussion

#### 5.1 Comparison with Other Algorithms

In this study, the accuracy of the locAP algorithm was higher than the accuracies of the three algorithms that are arguably most used clinically today (Milstein’s [12], Fitzpatrick’s [11] and Arruda’s [10] algorithms), as can be seen in Tables 4 and 5. The locAP algorithm also performed better than the other algorithms in a purely prospective study population (Table 6). Fur-
thermore, the other algorithms use a very limited number of locations. Milstein’s algorithm for example only uses four distinct locations, whereas locAP is the only known algorithm for localizing the accessory pathway that uses all 13 locations that were suggested in a consensus statement of the Cardiac Nomenclature Study Group, the Working Group of Arrhythmias, the European Society of Cardiology and the Task Force on Cardiac Nomenclature from the North American Society of Pacing and Electrophysiology (NASPE, now Heart Rhythm Society (HRS)) for this purpose [15].

Another advantage of the locAP algorithm is that it not only provides one single result, but a lot more information which the physician can interpret:
- the locAP score,
- the next most likely locations, and
- the locAP scores of the next most likely locations.

A software application using the locAP algorithm can also schematically display the 13 locations using a color coding that shows the likelihood that the accessory pathway can be found in this location. An example of the results screen of such a computer program is shown in Figure 4. Hence, the physician is not only provided with one final result, but he or she also gets additional information in order to help with the interpretation of the result.

Note that the locAP algorithm is the only known algorithm that uses the delta wave morphology only, without any additional criteria that would have to be observed additionally by the physician.

The locAP algorithm was developed in order to be used within a computer program. Personal computers, laptops, personal digital assistants and smartphones are widely available in today’s clinical routine, thus the usage of a computer program is easily feasible in clinical practice. As the computation of the accessory pathway is fast and can virtually be considered “real time”, using this algorithm instead of a manual, tree based algorithm is more time-efficient, in addition to the higher accuracy and the gain of additional information.

A score based algorithm has some advantages over a tree based algorithm. A tree based approach provides a final and definite result even for a meaningless input where the user cannot judge from the result alone whether this is useful or not (the result will not be useful for a meaningless input). A score based approach, however, would in such a case deliver a deterministic, but obviously meaningless result (e.g., low scores, regions with higher and lower scores mixed). If the user is unsure about a particular delta wave morphology, the morphology of that lead can be set to “unknown”, leaving this lead out of the computation of the locAP score. This is not possible in a tree-based algorithm, where the user would have to make a decision about an unclear delta wave morphology, potentially leading to a misclassification. Moreover, a tree based approach usually builds on pairwise, rather qualitative distinctions, that might not always be available. In a nutshell, a score based approach is more quantitative than a tree based approach.

A caveat is that very high accuracies were reported in the original studies of the other algorithms in use. For example, M. S. Arruda and co-workers reported an accuracy of 0.90 for their algorithm [10]. Such high accuracies could not be observed for these algorithms in this study. The observation that the published algorithms do not match their published accuracies (when applied by other groups) is shared by another study that compared three algorithms in current clinical usage [19].

Boersma and co-workers reported that algorithms to detect the accessory pathway often perform worse when applied to pediatric patients than when applied to adults [20]. For this study, however, the accuracies achieved with locAP in the entire population are similar to those achieved in the pediatric subset of the population (e.g., 53% accuracy for the entire population of 186 patients, and 55% for the subset of 20 pediatric patients).

### Table 4 The accuracies of locAP, Milstein’s, Fitzpatrick’s and Arruda’s algorithms

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Locations</th>
<th>locAP</th>
<th>Milstein</th>
<th>Fitzpatrick</th>
<th>Arruda</th>
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<td>0.60</td>
<td>0.50</td>
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</table>

* used localization pattern  
* number of locations

### Table 5 The accuracies of locAP, Milstein’s, Fitzpatrick’s and Arruda’s algorithms using all 186 data sets, including those with narrow QRS complexes and long PQ intervals

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Locations</th>
<th>locAP</th>
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### Table 6 The accuracies of locAP, Milstein’s, Fitzpatrick’s and Arruda’s algorithms using the 50 data sets of the prospective study population

<table>
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### Table 7

A cross table with the observed frequencies. The classifications by the locAP algorithm are displayed in the columns, the ablation sites are displayed in the rows.

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### 5.2 Clinical Importance

Being able to predict the location of the accessory pathway from the surface ECG is a valuable tool for a cardiac electrophysiologist. It allows a quicker catheter ablation procedure and a better risk evaluation before the procedure. A positive likelihood ratio of 24.94 proves that the locAP algorithm is a valid tool for predicting the location of the accessory pathway, since tests with positive likelihood ratios >10 are considered to provide large changes from pre- to post-test probabilities (i.e., the tests are highly useful) [21, 22].

If a software application is used, the following approach is suggested: If the most likely location’s locAP score is considerably higher than the next highest scores, it is very likely that the accessory pathway actually lies in this location. If the first two or three scores are similar and the associated locations are adjacent, it is very likely that the accessory pathway lies in this neighborhood. If none of the above is the case, it is likely that a region with a high concentration of red colors instead of blue colors (assuming a “rainbow” color scale) in the schematic LAO illustration holds the accessory pathway (Fig. 4).

### Table 8

Sensitivity, specificity and positive predictive value

<table>
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<tr>
<th>loca</th>
<th>sensb</th>
<th>specc</th>
<th>ppvd</th>
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<tr>
<td>Total</td>
<td>0.84</td>
<td>0.97</td>
<td>0.61</td>
</tr>
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</table>

*location
*b sensitivity
*c specificity
*d positive predictive value

This approach is justified for several reasons. The higher the locAP score, the higher is the likelihood that the accessory pathway is actually located there: the mean locAP score for a correct localization was 11.51 over a mean locAP score of 7.92 for an incorrect localization (p = 0.0004). The accuracy for the three most likely locations combined was 0.82, while 71% of the accessory pathways were located within the direct neighborhood of the most likely location. It can be observed from Table 7 that incorrectly classified locations very often lay near the actual ablation site. For example, LAL is classified as the most likely location 30 times. This is correct 20 times. Four times, the actual ablation site is LL, which is a direct neighbor of LAL. Additionally, the ablation site is LPL three times, which is also reasonably close to LAL. Thus, it is very likely that the accessory pathway actually lies in the region or neighborhood with the most likely location(s), shown as red colors in the schematic illustration (Fig. 4).
5.3 Study Limitations

A limitation of this study is that the results of this algorithm need to be interpreted by the physician; if a better accuracy than the “standard” accuracy of 0.54 is desired. This interpretation allows, of course, for subjective misinterpretations. Still, the additional information that is provided by the locAP algorithm should minimize the likelihood of misinterpretations. Furthermore, even the “standard” accuracy is higher than the accuracy of other algorithms in use that do not provide any information in addition to the algorithm result.

Due to logistic reasons, Milstein’s, Fitzpatrick’s, and Arruda’s algorithms were applied by an expert who is also an author of this study. However, this expert was unaware of the actual site of the accessory pathway when applying the algorithms, and therefore the application was unbiased.

Finally, localizing the accessory pathway using the delta wave morphologies from the surface ECG has some limitations in spatial resolution in its own account. The orientation of the heart in the thorax may be different for different patients and this influences the surface ECG. Thus, the delta wave morphologies will not be consistent for all patients with the same location of the accessory pathway. Evaluating all 13 locations, however, gives the physician a good insight into the likeliness of all locations and counteracts the surface ECG’s limitations. Multiple accessory pathways would alter the surface ECG, too. However, the prevalence of multiple pathways can be considered to be low. Note that not a single patient with multiple pathways was reported in this study, out of a study population of 186 patients who all possessed an accessory pathway. In such very rare cases where locAP’s easy and quick to use approach such as noninvasive imaging of cardiac electrophysiology might be used [23–25].

6. Conclusion

The locAP algorithm can help cardiac electrophysiologists in the planning process for catheter ablation procedures, especially if the locAP algorithm is applied using a software application. It could be shown that the newly developed locAP algorithm is a valid and valuable tool in a clinical setting. It could also be shown that usage of the locAP algorithm is favorable over the localizing algorithms that are in clinical use today.

Acknowledgments

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Disclosures

G. Fischer and F. Hintringer are partners at AFreeze GmbH.

References