Non-invasive three-dimensional localisation of arrhythmogenic foci in Wolff-Parkinson-White syndrome and in ventricular tachycardia by radionuclide ventriculography: phase analysis of double-angulated integrated single photon emission computed tomography (SPECT)

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Abstract
A new tomographic technique combined with phase analysis was used to detect premature and ectopic ventricular contraction patterns in 15 patients with Wolff-Parkinson-White syndrome and during ventricular tachycardia in seven patients. Data generated by gated single-photon emission computed tomography (SPECT) were analysed by backprojection of the Fourier coefficients, double-angulation, and integration to thick slices containing the ventricles, thus allowing visualisation of the contraction patterns in three perpendicular views. The results were compared with those of catheter mapping.

In nine patients with Wolff-Parkinson-White syndrome the site of initial contraction detected was identical with the site of the accessory pathway found by catheter mapping. The sites of origin of the ventricular tachycardias determined by catheter mapping were within 3 cm of the sites detected by the new technique. This new technique seems to be a promising non-invasive method for localising ectopic ventricular activity that will considerably shorten the time required for subsequent invasive procedures.

The exact site of the accessory pathway must be identified before patients with Wolff-Parkinson-White syndrome (WPW syndrome) can be treated with catheter ablation. Similarly, the detection of the site of origin of tachycardia is essential for intraoperative or catheter ablation in patients with sustained ventricular tachycardia. Invasive catheter mapping is the standard method used to localise accessory pathways in WPW syndrome and identify the site of origin of ventricular tachycardias before interventional procedures. It is difficult to localise anterograde conducting accessory pathways from the surface electrocardiogram. Also the determination of the origin of ventricular tachycardias from the configuration of the surface electrocardiogram is inaccurate. We and others have shown that phase analysis of radionuclide ventriculography is able to show the local contraction pattern and thus the site of initial contraction. If mechanical contraction follows the electrical excitation, localisation of ectopic ventricular depolarisation is possible. When phase analysis of planar radionuclide ventriculography was used to localise ectopic ventricular excitation in WPW patients and in patients with sustained ventricular tachycardia the results correspond well with the results of invasive mapping. In contrast, experimental data showed that this method is only able to detect an expanded area of initial contraction because the ventricles are displayed separately in only one projection (left anterior oblique). Even in this projection other cardiac structures are superimposed on the ventricles. In a previous study we reported the preliminary results of single-photon emission computed tomography (SPECT) and integrated slices that provide three dimensional cross sectional images of the heart derived from phase analysis. In addition to the left anterior oblique view of conventional planar phase analysis, an axial view of the heart was generated, which was perpendicular to the long axis of the body. This study reports on the first clinical data of phase analysis of radionuclide ventriculography obtained with a newly developed computer algorithm for analysing gated SPECT data. The method allows images to be generated in any projection of the cardiac blood pool with isolated display of the ventricular chambers.

Patients and methods
CONTROL GROUP
Forty patients with normal atrioventricular conduction in the surface electrocardiogram
made up the control group. Double-angulated integrated SPECT was performed during sinus rhythm to assess left ventricular function.

PATIENTS WITH WPW SYNDROME
We studied four women and 11 men (41-9 (13-9) 25-71 years). All of them had a delta wave in the surface electrocardiogram. Seven of them were studied during preexcitation of the ventricles caused by depolarisation through the accessory pathway and also during normal atrioventricular conduction with a narrow QRS complex: six patients after administration of ajmaline (50 mg intravenously) and one after successful catheter ablation.

In 14 patients catheter mapping was performed during an electrophysiological study and the atrial insertion of the accessory pathway was determined by the following criteria: shortest P—delta interval measured during stimulation with the mapping electrode, shortest VA interval during atrioventricular reentrant tachycardia and shortest VA interval during ventricular pacing. In all patients the whole atrioventricular ring was scanned by the mapping electrode to detect multiple bypass tracts. In one of these patients, catheter mapping could not be performed during the first mapping procedure because repeated atrial fibrillation episodes were induced mechanically by the mapping catheter. In two patients (case 19 and case 16) successful radiofrequency catheter ablation of the atrial bypass insertion was performed.23

PATIENTS WITH VENTRICULAR TACHYCARDIA
Only patients with haemodynamically well tolerated ventricular tachycardias were investigated. The mean (SD) age of the patients was 56-3 (12-2) years. Atrial fibrillation was noted in six patients, one had right ventricular dysplasia with areas of fatty degeneration in the left ventricle and in the septum detected by magnetic resonance imaging. In all but one patient two radionuclide studies were performed—during clinical ventricular tachycardia and then during sinus rhythm. Table 1 shows the details of these patients. The mean ejection fraction measured from left ventricular angiography was 39-3 (14-8)% (24-68%). The mean ejection fraction during tachycardia was 27-3 (7-7)% (17-38%) as determined by planar radionuclide ventriculography. The mean rate of the ventricular tachycardias was 152 (19) min (120-175/min). In all patients the origin of the tachycardia could be detected invasively, either by catheter mapping or by intraoperative mapping (case 4). All patients presented with one clinical ventricular tachycardia. Two patients showed another configuration of a non-clinical ventricular tachycardia. The site of origin of the clinical tachycardia was determined by the detection of a mid diastolic potential and by pace-mapping.4 A diastolic potential during tachycardia was found in six patients, and preceded the QRS complex by 60 ms (15-100 ms) on average. The criterion of pace mapping was fulfilled when the QRS complex paced by the mapping catheter was identical in more than 10 of the 12 surface leads with the configuration of clinical tachycardia on the electrocardiogram. This occurred in three of the patients. In three patients (cases 2, 3, and 7) catheter ablation was performed, in two of them (cases 3 and 7) by radiofrequency catheter ablation and in the other (case 2) by direct current.25 In one patient (case 4) the tachycardia could be tolerated haemodynamically for 20 min only after long-term administration of amiodarone. In this patient the site of origin of the clinical tachycardia was determined intraoperatively during surgical ablation.

MODE OF INDUCTION OF THE VENTRICULAR TACHYCARDIA
In all patients with ventricular tachycardia the tachycardia was induced directly after a basic control electrophysiological study and the stimulation was delivered through a catheter placed in the apex of the right ventricle. Single or double premature stimuli were used.

Table 1 Details of patients with ventricular tachycardia

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Disease</th>
<th>EF (SR) (%)</th>
<th>EF (VT) (%)</th>
<th>VT rate (min)</th>
<th>VT configuration</th>
<th>ORS (ms)</th>
<th>Axis (°)</th>
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<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>55</td>
<td>CAD</td>
<td>37</td>
<td>29</td>
<td>150</td>
<td>LBBB</td>
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</tr>
<tr>
<td>2</td>
<td>M</td>
<td>70</td>
<td>PW-An</td>
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<td>21</td>
<td>171</td>
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<td>+110</td>
</tr>
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<td>M</td>
<td>32</td>
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<td>150</td>
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<td>-90</td>
</tr>
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<td>M</td>
<td>56</td>
<td>CAD</td>
<td>24</td>
<td>38</td>
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<td>LBBB</td>
<td>180</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>58</td>
<td>AW-An</td>
<td>37</td>
<td>26</td>
<td>120</td>
<td>RBBB</td>
<td>180</td>
<td>-60</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>67</td>
<td>AW-An</td>
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<td>PW-An</td>
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<td>17</td>
<td>142</td>
<td>RBBB</td>
<td>170</td>
<td>+100</td>
</tr>
</tbody>
</table>

The mean (SD) ejection fraction measured by angiography during sinus rhythm is 39-3 (14-8)%). Mean ejection fraction during tachycardia (planar radionuclide ventriculography) is 27-3 (7-7)%). In patient 4 planar radionuclide ventriculography could not be used to determine the ejection fraction during ventricular tachycardia because of poor haemodynamic tolerance.

AW-An, anterior wall aneurysm; CAD, coronary artery disease; PW-An, posterior wall aneurysm; RVD, right ventricular dysplasia.
netium 99m pertechnetate we performed ECG-triggered 180° SPECT with a 64 matrix, 32 angles, 15 s acquisition per step and 8 frames per cycle (single-headed camera: Orbiter, Siemens). Fourteen minutes of active data acquisition was needed and six minutes for the deposition of the data. The parameters mean (zero harmonic), sine, and cosine coefficients of the first harmonic were extracted by Fourier analysis and back-projected. All pixels were then re-aligned along the long axis of the left ventricle (hence double-angulation). Four defined projections (those chosen for angiography and echocardiography) were calculated. Mean, sine, and cosine coefficients were added (integrated) to form thick slices that contained the complete ventricle under investigation. The integration was performed for each of the four chosen views (fig 1). This view dependent addition of voxels means that the images represent a projection of the corresponding view rather than a single slice. Finally, we calculated the phase values from each pixel (fig 2). In summary, these procedures result in planar scans of the heart in three projections. In this way, the contraction patterns and initial inward motion of each cardiac chamber was assessed separately without significant overlap of other cardiac structures.26

We performed conventional radionuclide ventriculography to calculate the ejection fraction after each SPECT investigation (see table 1). Two investigators who were unaware of the results of the catheter mapping procedure independently evaluated the frames of double-angled integrated SPECT.

**LOCALISATION OF ACCESSORY PATHWAYS BY DA-ISPECT**

Figure 3 shows the eight different areas along the atrioventricular ring that were used to localise the accessory pathways. The results were compared with those from catheter mapping. When the sites were identical the correlation was 2, when the sites were adjacent the correlation was 1 and in all other cases the correlation was 0.

**LOCALISATION OF THE ORIGIN OF VENTRICULAR TACHYCARDIAS BY DA-ISPECT**

We used a detailed diagram suggested by Kuchar 1989 that divides the left ventricle into 24 different areas (fig 4) to localise the origin of the ventricular tachycardia within the left ventricle. The results from catheter mapping were compared with those from DA-ISPECT. We attempted to measure the distance between the origin of the tachycardias as determined by catheter mapping and

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**Figure 1** Double-angulated integrated SPECT (DA-ISPECT). Schematic display of the zones of integration (addition) after double angulation according to the long axis of the left ventricle. These zones are depicted non-darkened in the upper part of the figure and are used to calculate the "thick slices" shown in the lower part of the figure. The projections are short axis view (SA), vertical long axis view for the right (RV-vLA) and the left ventricle (LV-vLA), and four chamber view (4CH).
Figure 2 Fourier phase images from DA-ISPECT. The projections are arranged as in fig 1. A colour code is shown on the right hand side. In the phase image the purple encodes the initial contraction and red the late contraction. The upper panel shows the contraction pattern in a healthy individual. There is early contraction (blue) at the septum (circle in the short axis view) and at the right free wall (circle in the long axis view of the right ventricle and four chamber view). The lower panel shows the contraction pattern in a WPW patient with an accessory pathway located anteroseptally (circle in short axis view and four chamber view). For the surface electrocardiogram see fig 8.

by DA-ISPECT.

All patients had given informed consent. The study complies with the declaration of Helsinki.

Results

CONTRACTION PATTERNS IN THE CONTROL GROUP

Sixteen (40%) of the 40 patients did not have a recognisable contraction pattern that reflected normal physiology. In 24 patients (60%) typical contraction patterns were seen. In five patients the initial contraction was seen at the anterior part of the right ventricle close to the apex (upper panel in fig 2). In four other patients the initial contraction was detected paraseptally at the right and left base of the ventricles. The remaining 15 patients showed a combination of these two patterns. This accords with the electrophysiological findings of electrical excitation during sinus rhythm. The early contraction in the right ventricle may be explained by a rapid propagation of the electrophysiological impulse through the moderator band.

CONTRACTION PATTERNS IN PATIENTS WITH ACCESSORY PATHWAYS

Table 2 shows the results in the WPW patients. Additionally, Kent bundle localisation from surface electrocardiogram was assessed by the algorithms of Milstein et al. and Gallagher et al.

Figure 5 shows the DA-ISPECT image for a patient (case 22) with a left lateral accessory pathway confirmed by catheter mapping. Because of a long effective refractory period, atrioventricular conduction along the accessory pathway could be blocked by intravenous ajmaline (50 mg), and a normal contraction pattern ensued (fig 5). Figure 6 shows the results of a DA-ISPECT study from a patient in whom catheter mapping identified a left posterolateral accessory pathway 3 cm distal to the ostium of the coronary sinus.

Four of the 15 patients had two accessory pathways. In one patient (case 17) no conduction could be detected from the ventricles to the atria through the accessory pathways. This patient had recurrent atrial fibrillation, resulting in rapid ventricular excitation through the bypass tract with rates of 250/min. The preoperative DA-ISPECT study did not show a distinct and consistent early contraction site (fig 7). During preoperative catheter mapping one accessory pathway was found posteroseptally 2 cm distal to the coronary sinus with an effective refractory period of 200 ms. During intraoperative mapping the atrial and ventricular insertion of the
Localisation of arrhythmogenic foci by SPECT

dias (260/min). Figure 8 shows the surface electrocardiogram. The surface electrocardiogram did not show a distinct site of an accessory pathway. The electrophysiological study showed an accessory pathway with a very short effective refractory period (180 ms). Localisation of the bypass tract was not possible because repeated mechanical induction of atrial fibrillation by the mapping catheter resulted in ventricular rates of 250/min. On one occasion induction of an atrioventricular reentrant tachycardia produced a left bundle branch block configuration with the same rate of 260/min, indicating an accessory pathway located on the right side or within the septum. A surface electrocardiogram recorded during maximum pre-excitation (rapid atrial stimulation) indicated a right lateral accessory pathway. The DA-ISPECT study showed clear evidence of early anteroseptal contraction (fig 2). Later, after oral administration of flecainide (300 mg/day), successful radiofrequency catheter ablation confirmed the presence of an accessory pathway located 1 cm anterior to the bundle of His. In the DA-ISPECT study after catheter ablation without pre-excitation, the beginning of the contraction could be localised posteriorly only—a small distance from the site detected by the first DA-ISPECT study. In patient 19, another successful radiofrequency catheter ablation confirmed the exact atrial insertion site of the accessory pathway. In patient 12 with two bypass tracts, the site of the second pathway was localised from DA-ISPECT only by retrospective re-evaluation.

Table 2 summarises the results. In 10 of the 14 patients in whom catheter mapping was performed the DA-ISPECT data correlated well with the catheter mapping data (fig 3). In three patients DA-ISPECT showed an area of early contraction next to the area found by catheter mapping. In one patient no correlation could be found between the two methods. In the four patients with two accessory bundles, only one pathway could be

accessory pathway was determined posterosseptally 1 cm anterior to the crux cordis. No further bundle was found. After operation intermittent atrioventricular conduction was seen with wide QRS complexes. The surface electrocardiogram indicated a second accessory pathway in the right lateral atrioventricular groove. The second DA-ISPECT study showed an initial contraction right posterolaterally during extensive pre-excitation (fig 7). The postoperative electrophysiological study showed a second accessory pathway at this site with an effective refractory period of 250 ms. However, this bundle was operating only intermittently, which is why it was not found during the preoperative and intraoperative electrophysiological examination. When the postoperative DA-ISPECT study was retrospectively re-evaluated two sites of early contraction caused by two accessory pathways became apparent (fig 7).

One patient with WPW syndrome (case 16) had atrioventricular reentrant tachycardia.

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Table 2  Localisation of initial excitation and contraction in patients with Wolff-Parkinson-White syndrome

<table>
<thead>
<tr>
<th>Case No</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>QRS duration (ms)</th>
<th>ECG Milsen*</th>
<th>Catheter (fig 3)</th>
<th>DA-ISPECT (fig 3)</th>
<th>Correlation* (2/10)</th>
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<td>(2)</td>
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<tr>
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<td>2 PS</td>
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<td>2</td>
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<tr>
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<td>M</td>
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<td>RL</td>
<td>—</td>
</tr>
</tbody>
</table>

Site of the accessory pathway determined from surface electrocardiogram according to Milsen et al: AS, anteroseptal; LL, left lateral; RL, right lateral; PS, posteroseptal; UD, undetermined. See fig 3 for designation of the site of the accessory pathways determined from catheter mapping and DA-ISPECT.

*Correlation: 2, same area detected by catheter mapping and DA-ISPECT; 1, area detected by catheter mapping was adjacent to the area detected by DA-ISPECT; 0, different areas detected by catheter mapping and DA-ISPECT.

†Successful radiofrequency catheter ablation.
CONTRACTION PATTERNS IN THE PATIENTS WITH VENTRICULAR TACHYCARDIAS

Table 3 shows the results in the patient group studied by DA-ISPECT during ventricular tachycardia. In two patients (cases 2 and 7) catheter ablation was not completely successful, though subsequent induction of the ventricular tachycardia was more difficult. The patients have not had tachycardia for 12 and 13 months respectively.

Figure 9 shows the results of a DA-ISPECT study in patient 2, who had an anterior wall aneurysm. The contraction patterns from phase analysis during ventricular tachycardia and during sinus rhythm were completely different. During ventricular tachycardia the contraction started in the mid-ventricle at the anterior part of the septum. This coincided with the origin of the tachycardia found by catheter mapping and was confirmed by catheter ablation. Figure 10 shows a DA-ISPECT study from a patient (case 6) with a posterior wall aneurysm and an ejection fraction of 33% during ventricular tachycardia. The initial contraction was located at the lateral side of the base of the left ventricle. Catheter mapping showed the site of origin of the ventricular tachycardia with a diastolic potential 100 ms before the QRS complex at the base of the ventricle, but this lay posteriorly, about 4 cm from the site of the initial contraction. In another patient (case 7) with a large anterior wall aneurysm (ejection fraction during ventricular tachycardia 17%) the site of origin of the ventricular tachycardia determined by catheter mapping was about 5 cm from the site detected by DA-ISPECT (table 3). The interpretation of the DA-ISPECT image was difficult because large areas showed early contraction in this patient. This was also true of patient 4, who also showed poor left ventricular performance. A second early contracting area (fig 4) was identified from the DA-ISPECT image.

In five of the patients the site of initial contraction accorded with the origin of the ventricular tachycardia (table 3). The differences seen in two of the patients will be discussed. The mean difference between the localisation of the focus by catheter mapping and by DA-ISPECT was 2·4 cm (range 1·5 cm).

Discussion

These are the first clinical experiences to be reported with the new method of double-angulated integrated SPECT. This new method of evaluating SPECT data has the advantage of showing ventricles in any chosen view. Difficulties, limitations, and possible clinical applications will be discussed for each patient group.

CONTRACTION PATTERN IN THE CONTROL GROUP

Only 60% of the control patients had a typical contraction pattern. This pattern of contraction corresponds to physiological excitation of ventricular myocardium via the
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His-Purkinje system, as reported for the human heart by Durrer et al. In the remaining control patients no distinct contraction pattern was identified. Even in 13 healthy dogs previously studied by DA-ISPECT, two animals showed contraction patterns that were different from physiological expectations. The contraction patterns in healthy individuals therefore seem to vary probably because of interindividual temporal variation in the electrical excitation of ventricular myocardium. This makes it more difficult to evaluate the results from the DA-ISPECT in WPW patients.

CONTRACTION PATTERNS IN WPW SYNDROME

Because there is no standard contraction pattern in controls, the investigator performing DA-ISPECT needs to know whether the patient being studied has a delta wave. In the clinical setting this information is always available. Each beat in a WPW patient with a delta wave is a combination of normal excitation along the His-Purkinje system and of excitation along the accessory pathway. The propagation of the earliest electrical excitation and ensuing contraction from the ventricular insertion site of the accessory pathway is slower than the electrical excitation along the physiological route (His-Purkinje system) which begins later. This makes it difficult to analyse the contraction patterns of such fusion beats. In seven of the patients the normal contraction pattern was seen when conduction through the accessory pathway was blocked (figs 5 and 6). This facilitated the analysis. In the WPW patients preexcitation was not increased by either pacing the atria or by drugs to broaden the delta wave. Pacing is an invasive procedure. Nevertheless, the effect of atrial pacing should be investigated to assess the diagnostic potential of DA-ISPECT in WPW patients paced from the atria.

CONTRACTION PATTERNS IN VENTRICULAR TACHYCARDIA

Compared with WPW patients preexcitation was always present during ventricular tachycardia and ventricular pacing (which was performed in two patients). This facilitates the evaluation of the DA-ISPECT results in the patients with ventricular tachycardia. We found a good correlation between the results of DA-ISPECT and catheter mapping regarding the site of origin of the ventricular tachycardia (table 3).

During the procedure of catheter mapping the pathway of slow conduction is localised...
by recording diastolic potentials and by other criteria. This small amount of electrophysiological activity in severely damaged myocardium does not lead to contraction. It is assumed that DA-ISPECT identifies healthy—that is—contractile myocardium that shows mechanical activity at the start of contraction. This may correspond to the site at the end of the slow conducting pathway a fact that may explain the difference between catheter mapping and DA-ISPECT results in patient 6. At present only invasive means such as catheter mapping (feasible in 16%) or mapping during surgery are able to detect the complete pathway of slow conduction.

In patient 4, who had an ejection fraction of only 17% during tachycardia, large areas of early contraction were identified. These may reflect areas of reduced contractility and could be the cause of the poor result of DA-ISPECT in this case.

Animal studies are needed to clarify the specificity of DA-ISPECT for identifying sites of excitation and subsequent contraction.

**ADVANTAGES AND DISADVANTAGES OF DA-ISPECT**

**Advantages of the DA-ISPECT in WPW patients**

- The results indicate that DA-ISPECT is more exact and reliable than the surface electrocardiogram in localising accessory pathways.

- It is non-invasive and though subsequent invasive procedures cannot be replaced by DA-ISPECT they are probably shortened by reducing the time required for fluoroscopy.

- Unlike DA-ISPECT catheter mapping usually identifies the atrial insertion of the accessory bundle. For catheter ablation of left-sided accessory pathways it is imperative to localise the ventricular insertion site because the atrial and ventricular insertions of the bypass tract may differ.

- DA-ISPECT can provide information in those rare patients in whom catheter mapping is not suitable.

- With DA-ISPECT there is only a little radiation exposure from the radionuclide.

**Advantages of DA-ISPECT in patients with ventricular tachycardia**

- DA-ISPECT takes less time than catheter mapping, it does not need an arterial puncture, and it is better tolerated by the patients.

- The resolution of the site of origin of the ventricular tachycardia is good enough for preoperative evaluation.

- Catheter mapping is contraindicated when a left ventricular thrombus is present.

**Disadvantages of DA-ISPECT in WPW patients**

- The success of DA-ISPECT is limited when the preexcitation is small (narrow delta wave).
Localisation of arrhythmogenic foci by SPECT

- In subsequent investigations preexcitation could be increased by pacing or drugs to improve the results of DA-ISPECT.
- The presence and location of multiple accessory pathways cannot be detected.
- Concealed bypass tracts are not detected. The functional properties of accessory pathways cannot be evaluated.

Disadvantages of DA-ISPECT in patients with ventricular tachycardias
- For data acquisition tachycardia must be induced by a stimulation catheter.
- The tachycardia must be tolerated for 20 min. This limits the number of patients in whom this method is suitable. Attempts to shorten the total time of data acquisition are in progress. The tachycardia rate can be reduced by drugs. This results in a better haemodynamic tolerance, as it does in patients who require catheter ablation.
- DA-ISPECT relies on mechanical contraction for the evaluation of excitation. But electrical excitation, which is recorded by catheter mapping, does not always lead to contraction.
- The success of DA-ISPECT is limited in patients with poor left ventricular performance.

Conclusions
Catheter mapping and intraoperative mapping remain the standard methods of localising accessory pathways and the origin of ventricular tachycardias. The results of DA-ISPECT are compared with the results of these methods. But in catheter mapping and even intraoperative mapping spatial discrimination is limited. The most exact method of localisation seems to be successful radiofrequency ablation, because it destroys small areas.

DA-ISPECT is a new method of evaluating cardiac blood pool SPECT. It has limitations and disadvantages in the evaluation of patients with arrhythmias. Nevertheless it is an additional tool to assess these patients before invasive procedures. In a few patients DA-ISPECT provides additional information that influences treatment (for example, in patients in whom atrial fibrillation is easily mechanically induced and in patients with thrombi). To date only a few patients have been investigated by DA-ISPECT. As the software becomes available to other centres, the method could be evaluated in more patients and its clinical usefulness could be determined.

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