Noninvasive recording of electrical activity in the PR segment in man

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SUMMARY A method is described for the noninvasive recording of electrical activity in the PR segment in man. Signals from chest surface electrodes, positioned on the basis of mapping experiments in 2 patients, were amplified 0.5 - 2.0 × 10^4 times and filtered to select frequencies from 40 to 500 Hz. Noise in the resulting signal was reduced using computerised digital averaging of 150 to 500 cycles. A time reference point, required for the averaging process, was derived from a change in slope of the QRS complex of a separate surface electrocardiogram. Digital filtering was used to eliminate high frequency residual noise after averaging. The system has been shown to recover the surface deflection resulting from a His pacing stimulus of only 20 mV. Highly reproducible electrical deflections were recorded in the PR segment in 2 healthy male subjects on whom the method was initially developed. Nine of 11 similar subjects subsequently showed recognisable patterns of activity within the PR segment. External recordings have been made in 10 patients undergoing simultaneous conventional His bundle electrography for conducting system disease. In 8, surface deflections have been obtained synchronous with the internal His waveform. In 6 cases, the configuration of internal and external signals was very similar. In 5 patients additional activity of interest was recorded late in the PR segment.

His bundle electrograms are of undoubted value in localising both the site of atrioventricular blocks and the origin of extrasystoles. They also help to characterise the electrophysiological effects of drugs on conducting tissue. The method by which His bundle electrograms are obtained is usually that of Scherlag et al. (1969) in which an intracavity electrode is introduced via the femoral vein such that two of its poles straddle the tricuspid valve. Alternative approaches using arm veins have also been described (Gallagher et al., 1973; Narula et al., 1973). The limitations and potential dangers implicit in the invasive nature of these techniques have, however, stimulated various workers to explore noninvasive methods of recording His bundle activity. Almost all have used signal averaging to extract meaningful activity from the noise of a highly amplified and filtered surface electrocardiogram (Berbari et al., 1973; Lazzara, et al., 1973; Stopczyk et al., 1973; Berry et al., 1974; Damato, 1974; Flowers et al., 1974; Berbari et al., 1975; Furness et al., 1975; Hishimoto and Sawayama, 1975; Ros, 1975; Akker, et al., 1976). Reported success in obtaining reproducible surface deflections which occur synchronously with conventionally recorded His bundle activity has varied widely. We have, therefore, sought to develop a system based on signal averaging which would give reproducible information in a high proportion of subjects, and to explore possible relations between the surface activity obtained in the PR segment and the intracavity His bundle electrogram.

Methods

(1) EXTERNAL RECORDING SYSTEM
Surface signals from the chest wall were sensed by disposable silver-silver chloride electrodes (Simonsen and Weel or American Optical) and were amplified by a purpose-built isolated preamplifier based on the integrated circuit OP-10 (Precision Monolithics Inc.). This device and its associated circuitry allowed a continuously variable gain of 0 to 10^4. The common mode rejection ratio of the preamplifier was 114 dB and noise level less
Noninvasive recording of electrical activity in PR segment in man

than 1 μV referred to the input. Its output was passed through a 40 Hz high-pass filter (Krohn-Hite Model 3202, 24 dB per octave, 'RC' response) and, after further amplification by a factor of 10, was recorded at 3-75 in/s on a 4-channel instrumentation recorder (Racal Store 4).

A simultaneous recording was made of the chest surface electrocardiogram without filtering and at a conventional amplitude by taking a signal directly to the recorder from an early stage in the preamplifier. This signal was used subsequently for timing in the averaging process.

On replay, the surface signal was passed through a 500 Hz low-pass filter (Krohn Hite Model 3202, 24 dB per octave, 'Max Flat' response) and was amplified sufficiently to bring the signal during the TP interval and PR segment to an average of ± 4·5 V. The additional gain required was 20 to 60 times, giving an overall system gain of 0·5 to 2·0 × 10⁶. Then followed the simultaneous conversion of surface and reference signals into digital form using a sampling rate of close to 4000 samples per second. The exact figure of 4000 and indeed any multiple of 50 Hz, mains frequency, was avoided.

Signal averaging was performed in a general-purpose computer (Modular One, Computer Technology Ltd.) using our own programme. The programme derived an accurate reference point in each cardiac cycle (required for the correct alignment of successive waveforms for averaging) from a change in slope of the QRS complex of the reference electrocardiogram. The rate of change of slope which determined the reference point could be chosen in each programme run to achieve maximum stability for any given signal. The programme displayed the reference electrocardiogram together with the derived reference point before averaging began and, if required, while the averaging was in progress. Optional facilities existed to display the new data being added into the average and to reject particularly noisy signals.

Any number of cardiac cycles could be averaged, but, since noise reduction is proportional to the square root of the number of cycles averaged, most of the improvement in signal-to-noise ratio was seen in the initial period of averaging. In most cases less than 250 cycles gave sufficient noise reduction.

The result of the averaging was displayed on a storage oscilloscope, drawn on an XY plotter, and produced in digital form on punched paper tape. If required, the averaged signal could be subjected to a low-pass digital filter within the computer before drawing, reducing the high-frequency noise and thus further improving the signal-to-noise ratio.

(2) ELECTRODE POSITIONS

We have performed mapping experiments in two patients undergoing conventional His bundle studies. In each, a bipolar subthreshold pacing stimulus was applied as close as possible to the bundle of His at a voltage sufficient to be sensed easily at the surface without averaging. Fig. 1 shows unipolar electrocardiographic recordings taken during the application of stimuli of 3 V amplitude. The 'active' electrode was sited sequentially at the positions shown, and the 'indifferent' input was the sum of the signals on each arm and the left leg throughout. The numbers adjacent to the traces indicate the surface voltage in mV of the inscribed pacing artefact (an average of 25). The optimum position is seen to be at the left sternal edge in the fourth intercostal space. Surface mapping with a bipolar configuration revealed that a signal of similar amplitude could be sensed at electrodes in each midclavicular line at the level of the fourth interspace.

The relation between these results and the unknown surface distribution of spontaneous His activity is open to question. The axis of the bipolar pacing electrode bore an uncertain relation to the anatomical axis of the common His bundle. Though the duration of the two signals was comparable, there was a distinct difference in the configuration (and probably also in the impedance) of the signals at source. Nevertheless, as in the work of Flowers et al. (1974) it seemed appropriate to use the optimum positions determined by mapping at least as an initial guide for placing electrodes in the search for surface activity in the PR segment.

(3) RECOVERY OF ARTIFICIAL SIGNALS

To test the sensitivity of the system, we have made unipolar chest surface recordings in 2 patients while applying 20 mV pacing stimuli close to the bundle of His at a rate of 130/min. The overall gain for the surface signals before averaging was 2·4 × 10⁶ and the reference point for the averaging programme was a short pulse from the stimulator (stimulus reference pulse), electronically separate from, but delivered synchronously with, the pacing impulse.

(4) RECORDINGS IN HEALTHY SUBJECTS

Surface recordings were made in 13 healthy male subjects aged 18 to 46 years, using the optimum bipolar electrode configuration. As the records were made in the computer room itself, 'on line' processing of the signals was possible without intermediate recording onto magnetic tape.


Figure 1: Conventional electrocardiographic traces showing the chest-surface signal at 5 unipolar electrode positions produced by a 3 v pacing stimulus applied close to the common His bundle. Numbers indicate the average amplitude in mV of 25 pacing spikes at each site.

(5) SIMULTANEOUS RECORDINGS OF EXTERNAL AND INTERNAL SIGNALS

Recordings of surface activity have been made in 10 patients undergoing conventional His bundle studies for suspected conducting system disease. All were in sinus rhythm. The internal His bundle electrogram was obtained readily in all cases by the method of Scherlag et al. (1969) using a bipolar electrode. A conventional electrocardiograph (Kent Cambridge Instruments Ltd., VS4) was used as a preamplifier for the internal signals which were subsequently displayed on a multichannel recorder (Cambridge Instruments Ltd.). The His bundle electrogram was recorded onto magnetic tape at 3-75 in/s simultaneously with the reference and filtered chest-surface signals from electrodes in the unipolar configuration. Electronic filtering identical to that used for the surface signals was applied to the internal signals on replay from the tape.

Results

(1) RECOVERY OF ARTIFICIAL SIGNALS

The result of averaging 200 cycles of chest surface signals during His pacing with a 20 mV stimulus is shown in Fig. 2. A representative cycle of the signal before averaging is shown in Fig. 2a in which all that is apparent is random noise. After averaging a clear spike emerged in a background of low voltage residual noise (Fig. 2b). Fig. 2c shows on the same time scale a direct record of the stimulus reference pulse, confirming synchrony between the applied stimulus and the surface activity. Since the His pacing was random with respect to the cardiac cycle and since the time reference for averaging was derived directly from the stimulator, the conventional cardiac waveform has been removed by averaging.

(2) RECORDINGS IN HEALTHY SUBJECTS

Eleven of 13 subjects showed recognisable activity in the PR segment, and in the 2 subjects on whom the method was developed this activity was found to be highly reproducible. An example is shown in Fig. 3, in which the top trace (S) is the surface recording after averaging and the lower trace is a simultaneous standard lead II. The surface record shows a sharp spike 45 ms before the onset of the QRS. A total of 5 subjects had a similar brief deflection occurring, as in this example, at a time when His bundle activity may be expected. Also inscribed is a later slower wave, a pattern shared by a total of 7 subjects. Three subjects had both early and late patterns, and 2 showed continuous polyphasic activity starting, respectively, 32 and 45 ms before ventricular activation.

(3) SIMULTANEOUS INTERNAL AND EXTERNAL RECORDINGS

In 8 of 10 patients deflections were inscribed in the surface record which were synchronous or near synchronous with the internal His activity. In 5 cases a later deflection was also recorded in the PR segment. Examples are shown in Fig. 4 and Fig. 5 in each of which a deflection occurs synchronously with the internal His deflection. In these and 4 other cases the configuration of the internal and external deflections was similar.

Discussion

At the body surface signals from the conducting system are no more than a few microvolts in
Noninvasive recording of electrical activity in PR segment in man

amplitude, and to record them is a formidable task. Unrelated electrical activity from skeletal muscle, the electrode-skin interface, and within the pre-amplifier is of a similar magnitude. Thus the high-gain amplification required to visualise tiny signals of interest inevitably results in overwhelming noise in which these signals become lost. However, by averaging together a number of successive cardiac cycles, random noise can be substantially reduced while repetitive activity related to the cardiac cycle is enhanced.

The usefulness of signal averaging depends critically on the provision of a constant interval between the signal of interest and the reference point by which successive cycles accumulating in the average are aligned. Berbari rejected all data in which variations in this interval ('trigger-jitter') could not be maintained to within at the most ± 2 ms (Berbari et al., 1973, 1975, 1976). Akker et al. (1976) quoted Uyen and Vendrik (1973) who consider that ± 1 ms is the upper limit of acceptable variation in this interval, and Furness et al. (1975) acknowledged that the low yield of surface PR segment activity he obtained was the result, in part, of unstable triggering.

Numerical estimates of triggering need careful interpretation. It may be unwise to assume that a constant interval between a QRS reference point and subsequent ventricular activation necessarily

![Fig. 2](image)

**Fig. 2** The recovery by signal averaging of the surface deflection produced by a 20 mV His pacing stimulus: (a) the chest-surface signal before averaging, (b) an average of 200 cycles, (c) a reference pulse produced by the stimulator synchronously with the pacing stimulus. This confirms the correct timing of the surface deflection recorded in (b).

![Fig. 3](image)

**Fig. 3** Surface deflections obtained from a healthy male subject by signal averaging. The averaged result (S) shows a 'spike' and a later, slower deflection within the PR segment. They begin, respectively, 45 and 18 ms before the onset of ventricular activation as recorded in a simultaneous standard lead II.
provides a sharper deflection from which to trigger and is more constantly related to His-Purkinje activity. However as the ventricular complex follows rather than precedes His bundle depolarisation, an arrangement must be made temporarily to store incoming PR segment signals until (and, if required, beyond) the time when the QRS trigger occurs. By continually refilling a large data array within the computer our programme retains digitalised signals for up to 1 second before the reference point is passed. The use of a flexible, digital system to define this point independently of baseline shift and early in the QRS complex has contributed to the high proportion of positive and reproducible results achieved in this series. The appearance of

indicates constant timing to the preceding signals of interest. Ros (1975) alone has reported the variability of the triggering interval between a QRS reference point and the internal His deflection and has obtained a figure as low as ± 0·7 ms. In the absence of a numerical estimate of triggering stability the recovery of high frequency signals after extended averaging suggests that triggering is acceptable since jitter causes increasing attenuation of high frequencies during the averaging process.

Early experiments to recover surface activity in the PR segment required atrial pacing to maintain adequate triggering (Berbari et al., 1973; Flowers et al., 1974). The atrial stimulator not only provided a sharp reference point but also, by maintaining a constant heart rate, fixed the interval between its impulse and subsequent His-Purkinje signals. To record conducting system activity by a method which avoids the use of intracavity electrodes we have used a surface electrocardiogram to obtain the reference point for averaging. The surface P wave is unlikely to provide good triggering because of its shallow configuration and because of the variability in AH interval with heart rate. The QRS complex

**Fig. 4** Simultaneous recording of a unipolar surface averaged lead (S), a conventional internal His bundle electrogram (HBE), and standard lead I in a patient undergoing investigation for conducting system disease. Note the appearance in S of a deflection synchronous with the internal His spike.

**Fig. 5** A second example of simultaneous PR segment activity recorded a surface averaged lead (S) and in the internal His bundle electrogram (HBE). Standard lead II is also shown.
high-frequency deflections in the averaged records also indicates that triggering is accurate.

There was a high rejection of mains interference in the averaged results. Records of surface activity could be made at the time of His bundle investigations in a conventional, unscreened catheter laboratory. The additional noise introduced by the magnetic tape recorder in studies away from the computer complex produced no adverse effect on the averaged result. In contrast intermediate magnetic tape recording was unnecessary for studies undertaken near the computer since the averaging programme reported earlier (Stroud et al., 1975), while flexible, is sufficiently fast for on-line processing.

Clinical evaluation of the His-Purkinje system requires measurement of the HV interval. The onset of the His deflection in a conventional electrogram is usually sufficiently clear for this measurement to be made without difficulty. In surface averaged recordings the onset of PR segment activity is often less easy to define. Extension of highly amplified atrial signals into the PR segment further obscures the onset of subsequent deflections and was the cause of our failure to retrieve clear PR segment signals in 3 cases. Though high-pass filtering reduces some components of atrial activity, we have found that attenuating frequencies above 70 Hz impairs the recovery of the PR segment signals. In addition, non-linear phase changes within the filter prolong the record of atrial activity into the PR segment. This effect is seen more prominently if the filter response is undamped and increasingly as its cut-off frequency is reduced or its slope of attenuation increased.

In this series we have obtained surface PR segment deflections of 19 of 23 cases. In 15 activity has been recorded at a time when depolarisation of the conventional His bundle would be expected. Similarity in timing between the surface events and the His deflection of a conventional internal electrogram has been shown in 8 of 10 patients having simultaneous internal and external recordings. These results add to the increasing evidence which suggests that external signals recorded in the PR segment are a result of His-Purkinje system activity. However, further improvements in technique are required before the system is of clinical value. Greater reduction in background noise and the suppression of unwanted atrial activity are needed to clarify PR segment deflections. A facility should exist to obtain a reliable reference point from the surface P wave as well as from the QRS complex to explore the possibility of recovering the conducting system activity in patients with complete infra-His block.

In conclusion we have described a sensitive system capable of recording recognisable PR segment activity in a high proportion of subjects by a method which is completely noninvasive. This activity may arise from depolarisation of the His Purkinje system, a concept supported by the close similarity in timing between the His deflection of a conventional His bundle electrogram and the early surface activity recorded simultaneously in 8 of 10 patients. Deflections late in the PR segment in 14 of 23 cases may contain potentially useful information hitherto unavailable by conventional His electrography. With further improvements in the technique and recruitment of microprocessing equipment it is conceivable that a bedside diagnostic instrument may be developed for recording conducting system activity in intact man.

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