Noninvasive Recording of His-Purkinje Activity in Man by QRS-Triggered Signal Averaging

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SUMMARY Mobile instrumentation and a clinically applicable method have been developed for external His bundle recording. High gain signal amplification (10^6) filtering (30–300 Hz) and averaging (128 or 256 consecutive cycles) are used. Acquisition of signals arising in the P-R interval is triggered by the patient’s QRS signal at the end of that interval. The precordial bipolar electrocardiogram is digitized at 5 kHz with 8 bit resolution and transferred to a 1,024 word, 18 bit signal averager. The averaged signal is then displayed on an oscilloscope and photographed. Good correlations were obtained between direct intracardiac and precordial recordings in experimental animals and in humans. Noise level after averaging was below 0.3 μV, and there was good elimination of asynchronous atrial and ectopic ventricular activity. With averaging of 128 or 256 consecutive cycles, the signal attenuation after propagation to the chest wall was in the range 1:2000 to 1:4000 in comparison with the directly recorded His bundle activity deflections. The noninvasive method may be of value in follow-up of acute and chronic disturbances of atroventricular conduction, as well as in studies of effects of pharmacologic interventions.

EXTERNAL RECORDING of cardiac conduction system potentials was first reported in 1973 by three independently-working groups of investigators. Berbari et al.1, 2 and Flowers et al.3 presented results of experimental animal studies and Stopczyk et al.4 and Lazzara et al.5 described recording in humans. Subsequent publications6-8 and studies from other laboratories9, 10 have confirmed the feasibility of external recording of the cardiac conduction system activity.

The externally recorded His bundle potentials were in the range of less than 10 μV. High-gain amplification was necessary to record the low magnitude precardial signals. Signal filtering and averaging was universally used to eliminate the random noise which was of similar magnitude. Since the signal-to-noise ratio increases with the number of averaged beats (repetitions), the averaging procedure usually required several hundred repetitions. The signal/noise relationship is described in the following formula:

(S/N)_m = \sqrt{m} (S/N), beat

(Where m = number of repetitions, S = signal amplitude, N = noise amplitude. For example, 100 repetitions are necessary to improve the S/N ratio by a factor of 10.) Large, general purpose digital computers have been utilized to perform this task on-line or off-line with the use of tape recordings.3, 5, 6, 8

The averaging method required synchronization of the R-R intervals for stable triggering, and an atrial pacemaker override was most commonly used.1, 2, 5, 6, 7, 8 The methods remained, therefore, partially invasive because of the need for introduction of an intraatrial electrode, and had only a limited advantage over direct recording of intracavitary His potentials.

Stopczyk et al.4 further modified the method by utilizing transesophageal pacing in human studies. Subsequently, Hishimoto and Sawayama10 reported on successful synchronization by utilizing the amplified P waves from the esophageal lead. These modifications made the method truly noninvasive for the vascular system.

Berbari et al.8 demonstrated in dogs that triggering with the QRS, utilizing specially designed QRS detector and digital computer, yielded results with consistent and reproducible morphology and timing. The external QRS-trigger averaged recordings compared well with those obtained by atrial pacing synchronization. Hishimoto and Sawayama10 utilized QRS synchronization in human studies by playing the magnetic tape recording of the precordial ECG in reverse.

We further modified the method to make it totally noninvasive and clinically applicable by: 1) eliminating the need for external pacemaker signal synchronization; 2) minimizing the required instrumentation; 3) obtaining an instantaneous display. In addition to developing the technique, the purpose of this investigation was to: 1) study the morphology of the filter-transformed cardiac signals; 2) study the influence of the averaging process on the His bundle potential recordings; and 3) compare the precordial recordings obtained by signal averaging with triggering by atrial pacing versus triggering with the patient’s QRS.
Methods

The His bundle potentials were recorded by using digital processing and averaging the amplified and filtered precordial electrocardiogram. The QRS serves as the trigger and provides a fiducial point for pre-trigger data acquisition and subsequent averaging.

A block diagram of the instrumentation is shown in figure 1. The system in its mobile mounting is shown in figure 2. The high-gain pre-amplifier (pre-amplifier A) for signal recording was selected on the basis of its very high signal/noise ratio.* It was most commonly used at a gain of 5–10 × 10^6. Bandpass filter settings of 30–300 Hz appeared optimal for rejection of the high amplitude, low frequency components (i.e., atrial repolarization or respiratory baseline drifts). A second pre-amplifier of the same type† (pre-amplifier B) with a bandpass filter setting of 10–30 Hz‡ and gain of 1–5 × 10^6 was used to provide the QRS trigger signal. The 10–30 Hz network acts as a differentiator, and the QRS trigger occurs when the slope of the signal exceeds a threshold value. The threshold is adjusted for consistent triggering at the time of recording.

The output of pre-amplifier A is amplified by a factor of 10, digitized at 5 kHz and stored digitally with 8 bit resolution in a transient signal recorder.‡ This is equivalent to 4 × 10^6 resolution. Using the pre-trigger mode of this instrument, a 204.8 msec window‡ preceding the QRS trigger is usually selected which includes the entire P–R interval as well as portions of the P and QRS complexes. Upon recognition of the QRS trigger from the pre-amplifier B, the contents of the digital memory (the pre-selected P–R interval) of the transient signal recorder are serially transferred to a 1,024 word, 16 bit signal averager.§ During this transfer, which takes 10 msec, the precordial ECG is not digitized. The averager allows continuous monitoring of the individual cycles or of the progress of the averaging process by its own front panel controls, as well as termination or further extension of the duration of averaging as desired. Upon termination of the process, the signals are displayed on an oscilloscope* and photographed with a Polaroid camera.

The precordial electrodes were placed in the third right and fourth left intercostal spaces parasternally. The triggering signal was obtained from the same set of electrodes. A separate grounding electrode was located elsewhere on the chest wall and its location varied. Standard, self-adhesive monitoring electrodes were used.† In addition, in some patients, a multiple electrode "local lead"§ was studied. The results confirmed its theoretical better discrimination of distant potentials as also noted by others. No definite superiority of this lead could be demonstrated for our purposes; its applications were somewhat cumbersome, and the system was abandoned during later studies.

Total system gain of 10^6 provides adequate resolution for our recordings. Accordingly, the photographed tracings typically have a gain corresponding to 0.5–4 μV per vertical division on the oscilloscope. Averaging 56 repetitions of known waveforms (triangular and sinusoidal) verified an overall system resolution of better than 0.1 μV.

In animal experiments (10 dogs) precordial recordings were obtained from a bipolar lead with electrodes located in the third right intercostal space along the sternal border (negative) and in the fourth intercostal space over the left lateral chest (positive). A multipolar recording catheter, introduced in the right atrium via the femoral vein, was used for simultaneous direct recording of the His-Purkinje system activity. The same procedure was followed in humans at

*Princeton Applied Research Model 113
†Biomation, Model 805 Waveform Recorder
‡This window can be extended to include longer time intervals, i.e., in first or second degree AV block
§Nicolet Instrument Corporation, Model 1072 with Model SD-78 High Speed Buffer Interface

*Tektronix, Model D10 Single Beam Oscilloscope with 5A24N Amplifiers
†Hewlett-Packard, Pre-gelled Disposable Electrodes (14245A)
the time of right heart catheterization in 10 patients. External recordings were obtained either simultaneously with the direct His bundle recording in the catheterization laboratory or on the same day in the noninvasive laboratory, if there was no documented alteration of the atrioventricular (AV) conduction on standard electrocardiogram. An additional 50 patients were studied without direct His bundle recording.

Results

Comparisons were made between: 1) the precordial averaged QRS triggered external His bundle (EHB) recording, and the direct intracardiac single-tracing recordings of the His bundle electrogram (HBE), 2) direct single HBE and HBE averaged from several consecutive cycles (utilizing intracardiac V spike triggering), to observe the effect of the averaging process on the directly recorded His spike; 3) averaged EHB triggered with QRS and EHB triggered by the atrial pacemaker spike, to observe whether there is any significant difference related to triggering by a theoretically less stable and less precise recognition of the triggering point on the QRS complex (due to the lower rate of rise and its amplitude) as compared with a sharp pacemaker spike. The ability of the recording system to eliminate the internal and environmental background noise was investigated. Also included were patients with nonsynchronous atrial activity such as atrial fibrillation or randomly occurring P waves in AV block and patients with ectopic ventricular activity.

Signal Transformation

Signal transformation during high-gain amplification and filtering results in marked changes of morphology from the standard electrocardiogram. High-gain amplification may reveal terminal potentials of atrial activation (including AV node) and earliest QRS potentials (i.e., Purkinje-myocardial junctions) not usually seen in standard electrocardiogram. Filtering eliminates the lower frequencies and differentiates the ECG curve, introducing additional deflections not present in the standard ECG tracing, shifting their peaks and accelerating the slopes.

The 30-300 Hz bandpass filter in the high gain preamplifier produces a time lag of approximately 11 msec at 15 Hz, and less than 4 msec above 30 Hz. Therefore, only very slowly varying signals would be appreciably shifted into the P-Q interval, and the H signal would be only minimally distorted.

Example of high frequency precordial ECG and high-gain filtered, averaged QRS triggered precordial ECG is presented in figure 3. In the single trace recording (upper tracing), the low frequency cut off is 0.3 Hz. The upper cut off of 300 Hz allows inclusion of higher frequencies, for possible earlier visualization of the QRS potentials. The averaged high-gain precordial recording (lower portion of the illustration) shows markedly accentuated deflections of the P, QRS and T waves due to differentiation of the original signal by filtering in the range of 30-300 Hz. The P-R interval including part of the QRS complex is seen in the left panels and the T wave and T-P interval is seen on the right. Comparison of the magnitude of individual deflections does not reflect the gain ratio (500:1) due to the process of differentiation by filtering as well as to partial cancellation of the voltages during the process of averaging (secondary to beat-to-beat variability of the deflections). There is no recognizable electrical activity during an interval of 50 msec between the end of P and the beginning of QRS in the upper tracing, while the lower tracing shows an additional early deflection which may represent the activity of the conduction system. A short segment of approximately 25 msec follows, during which only minor oscillations of the baseline are recorded. The T wave (right upper panel) has a duration of approximately 180 msec (note different time scale), followed by a mild downslope of 60 msec duration and P wave lasting 90 msec, (similar to that seen on the left side of the illustration). Averaging (right lower panel) introduced distortion of the T wave configuration. Assuming, however, that the T wave had the same duration of 180 msec and the P wave had its onset 60 msec later, there is evidence of electrical activity
between the end of the T wave and the beginning of the P wave.

Background Noise Including Asynchronous Cardiac Activity

As expected, high-gain amplification results in visualization of additional deflections not routinely seen in standard electrocardiogram, representing the activity of the cardiac conduction system. Small amounts of background noise originating from the recording system, leads and muscle potentials are inevitable. Direct measurements revealed that the magnitude of noise from the recording system and leads did not exceed 0.1 to 0.3 μV. Noise arising from muscle potentials was reduced to comparable levels after averaging 256 beats.

Figure 4 illustrates a recording obtained in a patient with third degree (complete) AV block, whose rhythm was controlled with an artificial ventricular pacemaker in the presence of asynchronous atrial activity. The recording system was synchronized to the ventricular pacemaker spike which was used as a trigger. Only minor oscillations of the baseline in the order of 0.1 μV are seen during 160 msec before the pacemaker spike. They are markedly lower than the deflections originating from the cardiac conduction system. Thus, the process of averaging is also adequate for eliminating the randomly occurring atrial activity. Equally good elimination of the ventricular extrasystoles was observed.

Animal Studies

A comparison was made in experimental animals between direct single beat recordings of the His bundle activity obtained with an intracardiac catheter and tracings obtained by precordial averaging. Examples are shown in figure 5. The upper tracings show intracardiac His spike of approximately 5 msec duration and 2 and 1 mV amplitude, respectively. The precordial averaged recordings (lower tracings) show deflections during the P-R interval of approximately 7 and 10 msec duration and 0.5 μV amplitude. Their beginning preceds the onset of ventricular activity by 20–25 msec, and coincides with that of direct recordings. Signal attenuation during propagation to the chest surface is in the range of 4000:1 and 2000:1. The duration of the averaged precordial His deflections appears slightly longer, and the deflections are less sharp.

Human Studies

Recordings obtained in human subjects are presented in figures 6, 7 and 8. Various comparisons
FIGURE 5. A comparison of single direct internal (upper tracings) and averaged external (lower tracings) recordings of His bundle activity in dogs. Direct recordings were obtained in a routine fashion using a multipolar electrode catheter. External recordings were obtained from the precordium by high-gain signal amplifications, filtering and averaging. Note different time scales in the left and right sides of the illustration. Intracardiac recordings show His spike preceding the V deflection by approximately 20-25 msec. External recordings show a major deflection preceding the beginning of QRS by a similar interval and coinciding with the internally recorded His bundle electrogram.

demonstrate that deflections representing activity of the conduction system can be easily identified in the precordial recordings.

Effects of the Signal Averaging Process

It is expected that filtering and averaging of the His signal recorded from the precordium will modify its configuration in comparison with direct intracardiac tracing by: 1) recording a more complete course of events than the bipolar lead from the endocardial contact electrodes; 2) signal differentiation through filtering and; 3) possibly beat-to-beat variation. Figure 6 shows comparison between the single intracardiac His bundle recording (fig. 6A) and averaged precordial recording (fig. 6C). The corresponding deflections are of 1 mV and 0.5 µV amplitude (2000:1 attenuation ratio) and precede the onset of ventricular depolarization by 35 and 31 msec, respectively. In the precordial recording the His spike is seen on the upslope of the baseline.

The effects of the averaging process on the direct intracardiac His bundle recording is presented in figure 6B. The averaging process was carried out in the same manner by triggering with the patient's ventricular activity deflection (V wave) recorded by the intracardiac catheter. A deflection corresponding to His bundle activity is seen during the P-R interval, with onset 29 msec before the beginning of ventricular activity. Comparison with the precordial recording shows similar temporal relationship and amplitude ratio of 2000:1.

Pre-trigger versus Post-trigger Signal Averaging

The comparison was made between the external recordings obtained by 1) triggering with an intratriatal pacemaker spike (post-trigger signal recording) and 2) triggering by the patient's QRS (pre-trigger signal recording). Figure 7A illustrates a single intracardiac His bundle recording. Biphasic His spike is seen with onset 47 msec before the beginning of ventricular activity deflection and an amplitude of 2 mV. Intraatrial pacing (with a rate slightly exceeding the spontaneous rate) was employed in figure 7B, and signals were averaged from the precordium. Pacemaker spike trigger synchronization resulted in biphasic His deflection of 2 µV amplitude (attenuation ratio 1000:1) preceding the QRS complex by 40 msec. The configuration of His deflections in single intracardiac and precordial averaged beats is very similar. Triggering with the patient's QRS (fig. 7C) and precordial averaging resulted in a His bundle deflection of approximately 0.8 µV amplitude.
FIGURE 7. A comparison of pacemaker triggering and triggering with the QRS on the averaged external recording of His bundle activity in man. Panel A shows a direct single beat intracardiac recording. His spike is seen preceding the beginning of V deflection by 47 msec and is of approximately 2 µV amplitude. Panel B shows external His bundle recording obtained with atrial pacemaker spike triggering. His deflection has an amplitude of 2 µV, and the beginning of its negative deflection precedes the beginning of rapid deflection of the QRS by 40 msec. Panel C represents averaged precordial His bundle recording synchronized by QRS trigger. The amplitude of the major His deflection is approximately 0.8 µV, and it precedes the first rapid deflection of QRS by 42 msec. (See text for discussion).

(Attenuation ratio 2500:1) with the onset preceding the QRS by 42 msec. It can be assumed that greater attenuation with QRS triggering is due to some degree of instability ( jitter) of the triggering point on QRS in comparison with pacemaker spike. However, the amplitude of His deflection is adequate to allow recognition and measurements of temporal relationships.

Clinical Studies

An example is presented in figure 8. This patient showed a day-to-day and hour-to-hour variation of AV conduction ranging from first degree AV block, Mobitz type I AV block and 2:1 AV block. The recording was obtained at the time when the patient’s electrocardiogram showed a first degree AV block with a P-R interval of 240 msec (fig. 8). Averaged precordial recording shows multiple deflections occurring during the interval of 120 msec, between the end of the P and the beginning of the QRS complex. A major deflection lasting 30 msec is seen approximately 80 msec prior to the onset of ventricular activity. The external recording is thus compatible with the first degree AV block associated with infranodal block (and possibly infranodal block as well because of the prolonged duration of the His deflection). Additional deflections are seen before and after the major His deflection, and they are also most likely related to the activity of the cardiac AV conduction system. Direct recordings were not available.

Reference ECG Lead

With improvement of the technique, our current clinical studies include a reference lead on the same photographic frame (fig. 9) to allow exact determination of the end of the P wave and the beginning of the QRS complex which otherwise may be difficult to recognize from the averaged precordial recordings. Double exposure on the Polaroid film is employed. Figure 9 includes averaged, high-gain filtered precordial electrocardiogram (His bundle recording) and a low-gain recording (top tracing) obtained from the same electrodes in a bipolar lead but with filter setting of 0.3–100 Hz, similar to that used in routine electrocardiography. Both tracings are recorded with the same QRS trigger to maintain full synchronization. On occasion, a third tracing is photographed (bottom, fig. 9) and it represents the same averaged His bundle electrogram, except for lower gain. Comparison of the
top and bottom tracings allows evaluation of the
degree of signal transformation due to filtering and
averaging.

**Discussion**

The major advantages of the method and system
used in our studies are the use of the patient’s QRS for
triggering, mobility of the equipment, simplicity of
operation, instantaneous readout and relatively low
cost. The method eliminates the need for external syn-
chronization (with atrial or esophageal pacing), tape
recording and data transfer and analysis by general
purpose computers.

Adequate quality recordings could be obtained in
the noninvasive laboratory as well as at the patient’s
bedside in the coronary care unit (with its multiple
monitoring equipment) and cardiac catheterization
laboratory. The instrumentation can be easily used for
serial examinations in patients who display instability
of the AV conduction, and it could possibly eliminate
the need for invasive studies in some patients.

The number of repetitions (consecutive cycles) of
128–256 appeared adequate for display of the conduc-
tion system activity. Low frequency filter cut-off at 30
Hz did not appear to influence the quality of record-
ings, but prevented the instability of the baseline
secondary to low frequency noise from electrode-skin
interface and respiratory variations. Upper frequency
cut-off of 300 Hz appeared not to lead to any loss of
conduction system signals, but prevented interference
from the equipment noise.

The baseline noise level after averaging did not ex-
ced 0.3 μV and the deflections originating from the
activity of the conduction system were well above this
level and were easily recognized. Similarly, the
averaging process was adequate to eliminate the ran-
domly occurring atrial activity. Repeated recordings
in the same subject during the same recording session
or on consecutive days showed good reproducibility,18
providing further proof that triggering with patient’s
QRS is adequately stable.

Major His deflections were well-seen in the
averaged internal (fig. 6) as well as external recordings
(figs. 5, 6 and 7). The process of signal averaging per-
formed on the direct internal recording of the His bun-
dle did not significantly change its morphology. A dis-
crepancy of a few milliseconds in the measured H-V or
H-QRS time intervals was noted (figs. 6 and 7). This
discrepancy is within the uncertainty of the measure-
ment and is not considered clinically important. Possi-
bile contributors to this uncertainty are trigger in-
stability and difficulty in defining onsets of H and V
signals in both the direct and high-gain precordial
recordings.

Comparison of external averaged recordings,
triggered with pacemaker spike and those triggered
with patient’s QRS (fig. 7) showed similar temporal
relationship of His activity deflection to the follow-
ing QRS, but the voltage of His deflection was slightly
higher in the pacemaker-triggered recording. The
cause of the attenuation of this deflection with QRS
triggering is not well understood. We assume that
some degree of variability of trigger point selection on
QRS existed, leading to partial cancellation of the
recorded voltage during the process of averaging. For
practical purposes, however, the magnitude of
recorded voltages appears less important for clinical
diagnosis than the temporal relationship, which is
similar in both types of recording.

On the basis of our experience with 150 studies in
experimental animals, normal subjects and hospital
patients, adequate recordings may be obtained in ap-
proximately 80% of cases.16 The reasons the deflec-
tions could not be well-identified in the remaining 20%
are not clear. Possibly the potentials generated in the
conduction system were small or their transmission to
the chest surface was impaired due to patient’s chest
configuration or other conditions, including
emphysema or obesity. Body position or incomplete
muscle relaxation usually was not a detrimental fac-
tor, at least in normal subjects. In fact, most of the
recordings during the early phase of technical evalua-
tion of the equipment and method were performed by the members of the research team on themselves while sitting, moving in the chair, conversing and making adjustments of the front panel knobs of the instruments.

Theoretically, it can be expected that the external recordings will encompass the whole spectrum of duration of the cardiac conduction system activity including the His bundle and its branches, as well as early deflections of ventricular activity including Purkinje-myocardial junctions. It is not known whether the activity of the AV node can be visualized, since it can be masked by the terminal forces of atrial activation. Experimental correlations will be required, including reproducing the pathology of the conduction system as well as effects of pharmacologic interventions. We recently suggested that utilization of the technique of high-gain amplification and averaging may allow visualization of the activity of the sinoatrial node in intra-atrial recordings. 

Our current experience indicates that, on occasion, several deflections are seen in the external recordings and difficulty arises in their identification and selection of the appropriate deflection for measurements of the H-V (H-QRS) interval (fig. 8). At present, the non-invasive method appears to be of value in acute disturbances of AV conduction, e.g., those secondary to acute myocardial infarction or for evaluation of sudden changes in the AV conduction after a previously mild chronic abnormality; for determination of the need for temporary or permanent pacing; in the long-term follow-up and study of the natural history of cardiac conduction system diseases. The noninvasive method may be an easy and practical way of evaluating the effects of various drugs on the conduction system. Generally, almost all indications for internal His bundle recordings may apply to the external technique except for those requiring single beat analysis, such as observations on the refractory period of the conduction system, or on sporadically occurring ectopic beats. These last conditions do not lend themselves to signal averaging.

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