ATRIOVERSION

MECHANISMS OF ATRIAL FLUTTER IN MAN AND A NEW TECHNIQUE FOR ELECTRICAL CONVERSION OF ATRIAL FLUTTER

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CONTENTS

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LIST OF TABLES

LIST OF FIGURES

Chapter 6

Chapter 7

Figure 7.6 A tachycardia is initiated by a high right atrial ectopic. The cycle length is identical with the ischaemic refractory period.

Figure 7.7 Activation maps for tachycardia of Figure A1.6.

Figure 7.8 Anatomical obstacles have been introduced. No tachycardia is induced, and only two echo beats follow the ectopic impulse.

Chapter 1

INTRODUCTION AND SUMMARY

This study evaluated the use of a new technique of intra-cardiac electrical stimulation of the heart, called Atrioversion. The unique feature of Atrioversion is the use of a stimulus having a very long pulse width. The technique was designed to be used for conversion of supraventricular tachycardia (SVT) to normal sinus rhythm. Conventional techniques of intracardiac SVT conversion use short stimuli, with a typical pulse width of 2 ms. These stimuli are designed to induce one or more ectopic beats during the tachycardia, which upset the electrophysiological balance existing during tachycardia, and thus terminate it. The stimulus delivered during Atrioversion has a pulse width which exceeds the cycle length of the tachycardia; the amplitude is above threshold level for depolarisation of the underlying tissue, and by using constant current, the stimulus stays above threshold throughout its duration. The objective in giving this long stimulus is :

1) to prematurely depolarise the stimulation site at the beginning of the impulse

2) to prevent a further depolarisation of that site by the continued passage of electrical current.

It is clear that if a further depolarisation can be prevented, and the stimulation site is within a reentry circuit which is responsible for perpetuation of the tachycardia, then the tachycardia should terminate. Consequently, two major problems were anticipated.

1) Is it possible to identify whether a stimulation site is within a re-entry pathway, before applying the long stimulus ?

2) How much current is required to **prevent**, rather than to cause, depolarisation of a stimulation site ?

The first problem will be further resolved by considering the response of the atrial flutter cycle length to the introduction of atrial premature beats at a given site, using conventional methods of electrical stimulation.

The second problem is more difficult to answer, because the marker of depolarisation is the local atrial electrogram, and this is often obscured during delivery of a long constant current pulse. In these cases, the current level required to prevent depolarisation can only be inferred from the level causing conversion of rhythm.

The study will look at the use of Atrioversion in the treatment of atrial flutter. It will demonstrate that Atrioversion is more effective than other methods of low energy electrical conversion in atrial flutter. The underlying mechanism of atrial flutter has been a subject of debate for some time, with opinions split between enhanced automaticity and circus movement reentry as the most likely cause. Observations made during the course of this study will be shown to support the concept that the underlying mechanism is macro-reentry, defined as reentry involving a mass of tissue large enough to be considered non-focal, and able to be investigated using intra-cardiac catheterisation.

Chapter 2

REVIEW

2.1 Therapy of atrial flutter

2.1.1 Introduction

The question of therapy for atrial flutter is a wide ranging one, covering not only termination of the arrhythmia, but also treatment of underlying heart disease or structural abnormalities predisposing to the arrhythmia; long term anti-arrhythmic prophylaxis is also included. This present study deals only with establishing a method for termination of atrial flutter, and therefore this section will only review other methods, past and present, aimed at the same end result : restoration of normal sinus rhythm. There are four main approaches which may be employed in the treatment of atrial flutter. These are:

1) Physical manoeuvres
2) Pharmacology
3) Electrical conversion
4) Ablation

2.1.2 Physical manoeuvres

These include carotid sinus massage (Josephson, 1974), eyeball pressure, breath holding, gagging, Valsalva manoeuvre, Mueller's manoeuvre and the facial cold pressor method (Waxman, 1980). All of these techniques are aimed at increasing vagal tone, and thereby lengthening refractoriness of, and slowing conduction in the sino-atrial (S-A) and atrioventricular (A-V) nodes. If the tachycardia involves either of these structures, it may slow and/or terminate. In atrial flutter, the degree of A-V block may increase; this can be a useful diagnostic tool in case of doubt as to the nature of the arrhythmia. All of these

techniques are simple to carry out, and should therefore be used as a first-line treatment; some can be carried out by the patient himself if an attack occurs out of hospital. However, the conversion rate is very low in atrial flutter (Braunwald, 1980, p.650).

2.1.3 Pharmacology

Acute drug therapy usually involves an intravenous injection of an antiarrhythmic agent specifically aimed at altering the electrophysiological properties of all or part of the tissue involved in maintenance of the arrhythmia. Different drugs have been developed with specific anti-arrhythmic actions; their differing modes of action have been classified (Vaughan-Williams, 1970), according to their effects upon the transmembrane action potential.

In atrial flutter, the most successful drugs are those which prolong atrial refractoriness and reduce conduction velocity, such as quinidine, disopyramide (Camm, 1981) and flecainide (Goy, 1986); unfortunately, these may first slow the atrial rate before conversion, and in some instances enhance AV conduction through a vagolytic effect, producing a paradoxical increase in the ventricular rate by decreasing the degree of A-V block. It may therefore be necessary to pre-treat the A-V node with, for instance, a beta blocking agent. Intravenous amiodarone may also be successful, and does not have the vagolytic effect of the above drugs (Strasberg, 1986). Other drugs are occasionally successful, but more frequently they increase AV nodal refractoriness and achieve better control of ventricular rate through an increase in AV block, without abolishing the atrial arrhythmia; digoxin and verapamil (Sung, 1980) fall into this category. Increased vagal tone may shorten atrial refractoriness, and this may play a part in the observation that flutter is often converted to fibrillation by digoxin. Beta blockers achieve a slowing of ventricular response by reducing sympathetic tone.

Apart from the low conversion rate, the main drawback of drug therapy is the toxicity of the drugs involved (Braunwald, 1980). All are potentially cardiotoxic, and most can have undesirable systemic side effects in addition. In a patient suffering side-effects, or frequent recurrences of tachycardia, a non-toxic method of conversion is to be preferred.

2.1.4 Electrical conversion

Electrical conversion of tachycardias has the advantage over pharmacology that, providing the method is reasonably quick, painless and non-traumatic, then it may safely be repeated as often as is necessary, without the worry of short or long-term toxicity. The history of electrical conversion methods will be reviewed.

2.1.5 Ablation

In the last five years, techniques have become available which allow a definitive treatment for atrial flutter. Endocardial catheter ablation (Scheinman, 1982) can be used to treat flutter by delivering a high energy synchronised shock through an electrode catheter to the region of the His bundle. This may cause permanent AV block (Evans, 1986), and obviate the need for chronic drug therapy or multiple hospital admissions. However, the patient requires implantation of a permanent cardiac pacemaker. Alternatively, Klein and Guiraudon (Klein, 1986) have described an open-heart operative procedure in two patients where cryogenic lesions in the region of the coronary sinus mouth and surrounding tissue abolished atrial flutter in short term follow-up; interestingly, one patient developed atrial fibrillation which was not previously observed. These techniques offer alternatives to chronic management of drug-refractory atrial flutter. The present study will address itself to acute conversion of the arrythmia.

2.2 Acute electrical conversion of atrial flutter

2.2.1 History

The first account of the use of electric current to terminate a cardiac arrhythmia dates back to 1899, when Prevost and Battelli (Prevost, 1899) defibrillated a dog by directly applied current. There was, however, no follow up of this work until Hooker (1933) and Wiggers (1940) demonstrated that direct defibrillation of the animal heart was possible using alternating current discharges with an amplitude of several Amperes.

2.2.2 Cardioversion

In 1956 an important new development occurred, with the advent of external electric countershock (Zoll, 1956). In the first instance, this involved the passage of high voltage, alternating current discharges to the thorax, in an attempt to completely depolarise the heart, and allow the sinus mechanism to resume. AC stimulation was found to be associated with a very high proportion of unwanted arrhythmias - ventricular fibrillation occurred in 20% of cases, and atrial fibrillation in 70% (Lown, 1964). In experimental animals, AC countershock produced myocardial damage in 90% of cases, with a 35% one-week mortality (Lown, 1964). The development of the much safer, and more effective, direct current countershock (Lown, 1962) began the modern era of defibrillation. A capacitor discharge was modified by a series inductor, to produce an underdamped sinusoidal waveform (the so-called Lown waveform), which thus limited the peak delivered current, and hence the myocardial damage caused. The defibrillator could be linked to a synchroniser unit, allowing the discharge to occur during the QRS complex of the surface electrocardiogram. This refinement meant that the discharge was not delivered during the ventricular T-wave, a period (known as the vulnerable phase) which was associated with an increased risk of inducing ventricular fibrillation (Zoll, 1962). This new method of treatment was called Cardioversion, and proved

very successful in dealing with all types of cardiac arrhythmias (Lown, 1963; Lown 1964; Oram, 1963).

Although cardioversion is a successful method, the large electrical currents which are delivered across the chest make the technique very painful to the patient, and thus a general anaesthetic is required. This, in itself, is associated with some hazard, and may be relatively contra-indicated in patients with cardiac or respiratory disease. It has also been noted that serious post-cardioversion ventricular arrhythmias can be induced (Lemberg, 1964), particularly in patients who are digitalised (Ten Eick, 1963).

In the therapy of atrial flutter, there is an even more fundamental objection to the use of cardioversion. A very large amount of electrical energy is delivered into the chest wall, of which only a small percentage dissipates in the heart (Lerman, 1986), and an even smaller percentage is needed to depolarise the atria, where the problem resides. It is clear that a direct approach would be more efficient in terms of energy delivery.

2.2.3 High energy intracardiac stimulation

Direct stimulation of the heart would suggest itself as a solution, and by using a venous electrode catheter, the procedure need involve no more discomfort to the patient than the administration of local anaesthetic to the venous access site. Recently, there has been considerable interest in the development of trans-catheter defibrillation (Mirowski, 1973) and cardioversion (Zipes, 1982). The implantable defibrillator can now provide effective out-of-hospital therapy for life-threatening ventricular arrhythmias, but is not indicated for atrial flutter (Mirowski, 1980). Zipes noted, in both animals (Jackson, 1982), and man (Zipes, 1982), that atrial arrhythmias could be terminated with a 1 Joule discharge from the implantable cardioverter. It should be remembered, however, that a 1 Joule shock will still have a peak amplitude of over 100 Volts, and will still be

painful. It would be preferable to use a technique involving lower energy stimuli, beneath the patient's threshold of pain.

2.2.4 Low energy intracardiac stimulation

As long ago as 1920, Sir Thomas Lewis (Lewis, 1920) postulated in his experimental studies that atrial flutter might be terminated by applying electrical stimuli, but he recognised the difficulties involved in precise timing and placement of the stimuli. Thirty five yeara later, 2 Volt stimuli delivered at between 1800 and 3600 stimuli per minute were shown to terminate atrial flutter in dogs (Lanari, 1955). It was suggested that this method might be tried in humans, but it was many years before this took place. In 1967 trans-catheter atrial pacing was first used for atrial flutter (Haft, 1967) and for supraventricular tachycardia with a 1:1 A-V response (Massumi, 1967). Since then, many authors have reported on their results, using various pacing techniques. The two major techniques of interest are :

1) Rapid atrial pacing

In this technique, the atrium is paced at a rate more rapid than that of the tachycardia. If the rate is fast enough, and the pacing is continued for sufficiently long, the tachycardia may be broken.

2) Extrastimulus pacing

A number of ectopic beats, usually between one and four, are induced by delivery of precisely timed and placed electrical stimuli. The timing of the stimuli is usually accomplished by using an intra-atrial electrogram as the trigger for a synchroniser, and introducing variable delays from the point of synchronisation, usually with an accuracy of 1 ms.

The use of these techniques will be discussed in relation to atrial flutter.

2.2.5 Atrial flutter - conversion using extrastimuli

Although flutter is highly sensitive to external Cardioversion (Braunwald, 1980, p.723), intra-cardiac stimulation methods have proved much less successful. It has been the experience of many authors (Massumi, 1967; Fisher, 1981; Wellens, 1980) that one or more extrastimuli delivered to the atrium during atrial flutter has proved unsuccessful in terminating the arrhythmia. This finding has been advanced (Wellens, 1980) as proof of the non-reentrant nature of atrial flutter. It is, however, possible that failure to convert was due to inadequately precise positioning of the catheter, as may be the case if a reentrant circuit exists and is anatomically small. Higher success rates have been reported on two occasions (Disertori, 1983; Gloor, 1986). Disertori had a 39% conversion rate to sinus rhythm using one or two stimuli and 77% using up to three stimuli. His stimulation protocol and location of a correct catheter position do not appear to vary greatly from accepted methodology, so it is difficult to explain why his success rate is high. Gloor found that single stimuli were effective in 13%, single or paired in 26%, and 1,2 or 3 stimuli in 45%. Atrial fibrillation was also induced in 10%. This latter study is the only one to describe conversion of flutter using a single atrial extrastimulus (in 5 patients).

2.2.6 Atrial flutter - rapid atrial pacing

Rapid overdrive pacing has been widely used as a treatment of atrial flutter, and has become the accepted alternative to cardioversion. The first report of this method came in 1967 (Haft, 1967). Four episodes of flutter were treated in three patients, using rapid atrial pacing at between 360 and 400 beats per minute. The results were conversion to atrial fibrillation twice (one episode

immediately converting to sinus rhythm), to sinus rhythm directly in one instance, and to a faster atrial flutter in one case. Subsequently, many other workers examined the feasibility of this method, and developed their own protocols for stimulation. A review of 24 papers on the subject is summarised in Table 2.1 (see table for references). It should be noted that the cases referred to in Table 2.1 are individual episodes of atrial flutter, and thus multiple but distinct episodes in the same patient are treated as separate "cases". In 505 episodes of flutter, sinus rhythm was regained 249 times (49.3%). Atrial fibrillation occurred 190 times (37.6%) and in 66 cases (13.1%) there was no change. 101 of the 190 cases of atrial fibrillation spontaneously returned to sinus rhythm within 48 hours, representing a spontaneous conversion rate of 53.2%. The total number of cases eventually regaining sinus rhythm was 350 (69.3%), and conversion of rhythm was achieved in 439 (86.9%). This last figure is of importance, because, even if sinus rhythm cannot be regained, a conversion to atrial fibrillation is generally considered favourable. The ventricular response to atrial fibrillation is more predictable and more easily controlled by drugs (eg digoxin) than is the response to atrial flutter, where near toxic levels of digoxin may not affect the AV conduction ratio. The difference in response is probably due to the effect of frequent concealed conduction (Josephson, 1979) of fibrillatory impulses into the A-V node, thus increasing its refractoriness without being conducted to the ventricle. Presumably, this effect is particularly enhanced by digoxin.

It can be seen that successful conversion rate varies widely from author to author. Three factors may help to explain this variation. These are:

1) Stimulation protocol

Some authors use extremely rapid stimulation - at up to 1200 beats per minute - and tend to induce atrial fibrillation. The more successful protocols tend to pace at rates only slightly in

Table 2.1

Atrial flutter and rapid atrial pacing

Author	Year	Cases	SR	AF (SR<48hrs)	(sust)	No change
Haft	1967	4	2	1	1	0
Lister	1968	2	1	0	1	0
Zeft	1969	10	6	1	0	3
Gulotta	1970	9	6	3	0	0
Zipes	1971	15	8	2	0	5
Cheng	1971	12	9	0	0	3
Rosen	1972	15	0	0	6	9
Vergara	1972	76	27	16	17	16
Puech	1973	29	12	10	6	1
Montoyo	1973	6	0	0	4	2
Mitsui	1973	2	0	0	2	0
Preston	1973	24	15	0	6	3
Pittman	1973	25	11	6	6	2
Orlando	1977	36	24	3	6	3
Waldo	1977	30	24	4	1	1
Murphy	1978	11	7	0	1	3
Das	1978	49	23	13	12	1
Watson	1980	38	34	0	4	0
Henthorn	1980	12	9	0	3	0
Camm	1980	10	2	0	2	6
Wellens	1980	49	0	38	7	4
Kerr	1983	10	8	0	0	2
Gloor	1986	19	11	4	2	2
Bertholet	1986	12	10	0	2	0
Total		**505**	**249**	**101**	**89**	**66**
			49.3%	**20.0%**	**17.6%**	**13.1%**

Total conversion rate	= 439/505	= 86.9%
Immediate conversion to SR	= 249/505	= 49.3%
Immediate conversion to AF	= 190/505	= 37.6%
Spontaneous return to SR	= 101/190	= 53.2%
Total conversion to SR	= 350/505	= 69.3%

Key:

SR	- sinus rhythm
AF	- atrial fibrillation
sustained	- AF sustained or requiring cardioversion

excess of the spontaneous flutter rate. Waldo (Waldo, 1977) limits the pacing rate to 125% of the atrial flutter rate. He states that exceeding 135% is associated with increased incidence of atrial fibrillation.

2) Patient selection - duration of flutter.

In patients who have had atrial flutter for long periods of time, or who have severe underlying heart disease, particularly mitral valve disease, atrial flutter tends to be difficult to convert to sinus rhythm. Several of the more successful series have studied patients whose flutter was either induced at electrophysiological study, or was of recent onset, often after heart bypass surgery. These flutters of recent onset are more easy to convert, as will be shown below.

3) Drug therapy

Many patients, particularly those whose atrial flutter is of long duration, are treated with digitalis. In some studies, this was stopped for at least 48 hours before attempting conversion. In other studies, conversion was carried out in the presence of digoxin. There was seen to be a difference in the results related to the use of digoxin (see below).

Table 2.2 summarises the results of rapid atrial pacing, in episodes of atrial flutter which were either induced, or had a duration of less than 24 hours. There is a high success rate for immediate conversion. In Table 2.3, the results are shown for flutter of greater than 24 hours duration. Table 2.4 compares the two groups; immediate success rate is significantly higher in flutters of shorter duration (74.1% vs. 47.6%; $p < 0.0005$). Furthermore, the total conversion to

Table 2.2

Rapid atrial pacing - flutter duration < 24 hours

Author	Year	Cases	SR (SR<48hrs)	AF (sust)		No change
Zeft	1969	5	1	1	0	3
Gulotta	1970	8	5	3	0	0
Rosen	1972	1	0	0	0	1
Orlando	1977	6	6	0	0	0
Waldo	1977	30	24	4	1	1
Watson	1980	38	34	0	4	0
Camm	1980	10	2	0	2	6
Kerr	1983	10	8	0	0	2
Total		**108**	**80**	**8**	**7**	**13**
			74.1%	**7.4%**	**6.5%**	**12.0%**

Table 2.3

Rapid atrial pacing - flutter duration > 24 hours

Author	Year	Cases	SR (SR<48hrs)	AF (sust)		No change
Haft	1967	4	2	1	1	0
Zeft	1969	5	5	0	0	0
Gulotta	1970	1	1	0	0	0
Rosen	1972	14	0	0	6	8
Puech	1973	29	12	10	6	1
Orlando	1977	30	18	3	6	3
Murphy	1978	11	7	0	1	3
Das	1978	49	23	13	12	1
Total		**143**	**68**	**27**	**32**	**16**
			47.6%	**18.9%**	**22.4%**	**11.2%**

Key:

SR - sinus rhythm
AF - atrial fibrillation
sustained - AF sustained or requiring cardioversion

Table 2.4

Effect of duration of flutter upon % conversion rate

	Duration of flutter	
	<24 hours	>24 hours
Total conversion rate	88.0	88.8
Immediate conversion to SR	74.1	47.6
Immediate conversion to AF	13.9	41.3
Spontaneous return to SR	53.3	45.8
Total conversion to SR	81.5	66.5

Immediate conversion to sinus rhythm is more likely if flutter duration is less than 24 hours
(chi-squared = 16.85, $p<0.0005$).

Total conversion to sinus rhythm is more likely if duration is less than 24 hours
(chi-squared = 7.12, $p<0.01$).

sinus rhythm (including spontaneous reversions from AF) was also higher in the first group (81.5% vs 66.5% ; $p<0.01$). This factor must be taken into account when assessing the effectiveness of any therapy, including the new technique outlined in the present study. Digoxin was also an important factor influencing immediate conversion to sinus rhythm. It was possible to ascertain the use or non-use of digoxin in 274 of the 505 episodes of flutter in the papers reviewed. In Table 2.5, it can be seen that conversion rate is 54.9% in digitalised patients, and atrial fibrillation occurs in 34.7%. In undigitalised patients (Table 2.6), immediate conversion is higher (69.3% vs 54.9% ; $p<0.05$). Overall conversion rate to sinus rhythm (including spontaneous reversion from atrial fibrillation) is not significantly different in the two groups. These results are summarised in Table 2.7.

2.3 The mechanism of atrial flutter

2.3.1 Introduction

The existence of the cardiac arrhythmia now known as atrial flutter went undescribed until 1911, when W.A.Jolly and W.T.Ritchie (Jolly, 1911) published their paper, entitled "Auricular flutter and fibrillation". The relatively recent discovery of this arrhythmia is explained by the difficulty in its differential diagnosis from atrial fibrillation using purely clinical examination, particularly if the ventricular response is irregular. The invention of the string galvanometer (Einthoven, 1907) allowed, for the first time, the electrical activity of the atria to be graphically recorded, and demonstrated that it was possible for the atria to beat regularly at rates much higher than had previously been imagined, indeed over 300 times per minute.

The classic electrocardiographic appearance of atrial flutter was first described by Sir Thomas Lewis (Lewis, 1920). He noted that the atrial activity showed a continuous, sawtooth-like undulation in leads II and III, but that the

Table 2.5

Rapid atrial pacing - patients on digoxin

Author	Year	Cases	SR (SR<48hrs)	AF (sust)		No change
Lister	1968	2	1	0	1	0
Zeft	1969	7	4	0	0	3
Gulotta	1970	9	6	3	0	0
Zipes	1971	11	5	2	0	4
Cheng	1971	12	9	0	0	3
Puech	1973	11	5	4	2	0
Pittman	1973	22	10	6	5	1
Orlando	1977	26	16	2	5	3
Murphy	1978	10	6	0	1	3
Das	1978	48	22	13	12	1
Henthorn	1980	12	9	0	3	0
Bertholet	1986	3	2	0	1	0
Total		**173**	**95**	**30**	**30**	**18**
			54.9%	**17.3%**	**17.3%**	**10.4%**

Table 2.6

Rapid atrial pacing - patients not on digoxin

Author	Year	Cases	SR (SR<48hrs)	AF (sust)		No change
Haft	1967	4	2	1	1	0
Zeft	1969	3	3	0	0	0
Zipes	1971	4	3	0	0	1
Puech	1973	18	7	6	4	1
Pittman	1973	3	1	0	1	1
Orlando	1977	10	8	1	1	0
Murphy	1978	1	1	0	0	0
Das	1978	1	1	0	0	0
Watson	1980	38	34	0	4	0
Camm	1980	10	2	0	2	6
Bertholet	1986	9	8	0	1	0
Total		**101**	**70**	**8**	**14**	**9**
			69.3%	**7.9%**	**13.9%**	**8.9%**

Key:

SR	- sinus rhythm
AF	- atrial fibrillation
sustained	- AF sustained or requiring cardioversion

Table 2.7

Effect of digoxin upon % conversion rate

	Digoxin	No digoxin
Total conversion rate	89.5	90.2
Immediate conversion to SR	54.9	69.3
Immediate conversion to AF	34.6	21.8
Spontaneous return to SR	50.0	36.4
Total conversion to SR	72.2	77.2

Immediate conversion to sinus rhythm is less likely in digitalised patients. (chi-squared = 3.99, $p<0.05$)

atrial complexes were usually very small in lead I (Lewis, 1925). There is no appreciable atrial isoelectric interval in the inferior leads, and of particular interest, he noted that traces taken from different patients suffering from atrial flutter often showed a remarkable similarity in the form of the atrial complexes. The atrial flutter described by Lewis is now usually referred to as the "common" form of atrial flutter. It has become apparent recently that another type of flutter exists, the "uncommon" form, in which the P-wave axis is completely different. The P-waves are usually positive in leads I,II and III. It has been suggested (Mirowski, 1967) that the atypical form of atrial flutter has a different mechanism to the common form, and that the two arrhythmias will therefore react differently to attempted conversion, either by electrical or pharmacological methods.

The mechanism which underlies atrial flutter has been a subject of controversy during the seventy years since it was first described. The two theories generally proposed are :

1) Enhanced automaticity

This theory suggests that there is a rapidly discharging ectopic focus somewhere in the atria, which is responsible for the rapid atrial rates during atrial flutter. The ectopic focus will be confined to a cell or a small group of cells, and may be inaccessible to an exploring intracardiac catheter.

2) Circus movement

The reentry concept suggests that there is a continuously circulating depolarisation wavefront, without a true origin, which circulates around an obstacle in the atria. The length of the wavefront will depend on the size and nature of the obstacle, which may be anatomical (eg the opening of a great vein into an

atrium) or functional (eg an area of depressed conduction in the atrial myocardium), or may be a combination of both. If the reentry circuit is very small, and cannot be investigated by catheter methods, then the mechanism is termed MICRO-REENTRY. If, however, the circuit "radius" is of the order of centimetres rather than millimetres, then the mechanism is MACRO-REENTRY. Micro and macro-reentry mechanisms may be functionally similar, but react differently when investigated by intra-cardiac catheterisation. Due to the smallness of a micro-reentry circuit, it may not be possible to distinguish it from an ectopic focus.

Any theory of the mechanism underlying atrial flutter must answer several questions.

1) Why is the P-wave axis on the surface electrocardiogram so similar in different patients with the "common" form of atrial flutter ?

2) How does this mechanism explain the response or non-response of atrial flutter to different forms of electrical and pharmacological stimulation ?

2.3.2 Enhanced automaticity - the focus theory

In atrial flutter, the atria beat very rapidly, typically 240 to 360 times per minute. In normal sinus rhythm, the heart rate is controlled by the sinus node, which spontaneously depolarises at a rate controlled by the autonomic nervous system. It is suggested that an abnormal ectopic focus elsewhere in the atria may be capable of spontaneous depolarisation at the rapid rates occurring

during atrial flutter. Prinzmetal (1952) cited atrial flutter as being focal in origin. His observations were based on chemically-induced flutter (topical administration of aconitine to the exposed rabbit atrium), which may not closely correlate with clinically occurring flutter (Kimura, 1954). His cinematographic studies showed radial propagation of the impulse away from the point of stimulation, and he suggested that the continuously undulating baseline during atrial flutter was not due to depolarisation throughout the atrial cycle, but was due partly to atrial repolarisation. Katz (1959) stated that a single parasystolic focus could not be ruled out as a cause of atrial flutter. One of the strongest proponents of the focal viewpoint is Scherf, whose paper in 1966 (Scherf, 1966) reviewed the available evidence, and came down strongly in favour of a focal origin for atrial flutter. He attempted to disprove the assumption that flutter is due to macro-reentry, by creating atrial flutter in the experimental dog by the method of Rosenblueth and Garcia-Ramos (Rosenblueth, 1947). This method uses rapid electrical stimulation applied to the atria, following mechanical crush of an area between the venae cavae; a persistent tachycardia can thus be provoked, which closely resembles spontaneously occurring atrial flutter. This tachycardia has often been referred to as "electrical flutter". If this arrhythmia is due to reentry around the venae cavae and/or the crushed area, then it should be terminated by interrupting the reentry circuit, either by tying ligatures, or by cutting. Scherf demonstrated that such cutting did not terminate the tachycardia (Scherf, 1954), and concluded that reentry was not present. He stated that the P-waves in atrial flutter always resembled the P-waves of the sinus or A-V nodal rhythms which preceded it, and that enhanced automaticity in one or other of these structures was probably responsible. Marques also carried out a similar experiment (Marques, 1962), and mapped the resultant arrhythmia using direct exploring electrodes, and showed a spread of excitation consistent with focal activity. Scherf has also described studies (Scherf, 1947) involving the

administration of irritant alkaloid substances, such as aconitine and delphinine, directly to atrial myocardium. Rapid beating results, which Scherf stated was similar to atrial flutter, and was unarguably focal in nature. This "aconitine flutter" may be produced by topical application at any point in either atria. Scherf suggests that electrical flutter is a different entity, although still focal in origin, but originating only in fibres of the sinus node or A-V node. This latter viewpoint is refined by Mirowski and Alkan, who state that vectorial analysis of the surface electrocardiogram in the common form of atrial flutter suggests a focus of activity low in the atria (because the P-waves are negative in the inferior leads) and probably in the A-V node (Mirowski, 1967). The P-waves in uncommon flutter are likely to originate high in the atria. Four cases of atrial flutter are described in this paper; the P-wave vector is said to suggest left atrial automaticity as the cause of the flutter. In support of a left atrial origin, the authors point out that atrial flutter is more likely to occur in conditions causing left, rather than right, atrial overload, such as mitral valve disease. Support for this theory is indirectly supplied by Hoffmann and Cranefield, who demonstrated automaticity in cells of the coronary sinus and at the left atrial junction with the pulmonary veins (Hoffman, 1964). Rosen further developed this idea by using rapid pacing of the left atrium and/or coronary sinus in dogs and healthy male volunteers (Rosen, 1969). Correct catheter positioning was assessed by the recording of inverted P-waves in lead II of the surface electrocardiogram, when pacing was performed through the catheter. At pacing rates of up to 250 beats per minute, discrete P-waves, separated by a clear isoelectric period, were seen. These P-waves were negative in leads II,III and aVF, and of varying morphology in leads I and V1; their axis was thus similar to the P-wave axis in the common form of atrial flutter. When the pacing rate was increased, the isoelectric period disappeared, and continuous undulation of the baseline was seen, closely resembling the electrocardiographic appearance of clinical atrial flutter. Rosen

suggests that some cases of atrial flutter may be unifocal in origin, and that this focus may be in the coronary sinus or low left atrium. Wellens studied atrial flutter in a man undergoing open-heart surgery (Wellens, 1971); direct exploring electrodes were used to map the epicardial surface of the heart during flutter. The patient had moderately severe mitral stenosis, and a much enlarged left atrium. Thirty-seven epicardial electrograms were recorded, and demonstrated "*earliest recordable atrial epicardial activity*" at the medial surface of the right atrial appendage, close to the aortic root (it could be argued that in the presence of a continuous undulating surface flutter wave, the concept of "earliest" is arbitrary, as there is no time reference point). There was more or less radial epicardial spread of activity from this point, and atrial activation spanned 192 ms, out of a flutter cycle length of 235 ms. It is known that epicardial activation does not mirror endocardial activity, and Wellens suggests that the discordant site of earliest epicardial activation, compared to those studies above, which postulate a low left atrial focus of activity, may be explained by rapid retrograde conduction along the anterior internodal tract. However, no evidence is put forward to support this idea. Wellens adds two caveats to his findings:

1) This study does not differentiate between focal activity and micro-reentry low in the atrium.

2) The conclusions apply only to this patient.

It might be suggested that no conclusions of any kind regarding endocardial activation and mechanism of atrial flutter can be drawn from a study of possibly unrelated epicardial activation, although the thin walls of the atria make it likely that the two will in fact be more closely related than is the case for ventricular mapping.

Wells discussed the effects of rapid atrial pacing upon spontaneously occurring atrial flutter (Wells, 1979), and was led to subdivide flutter into:

> **TYPE I** : with atrial rates below 340 beats per minute, and sensitive to conversion using rapid atrial pacing.
>
> **TYPE II** : with atrial rates above 340 beats per minute, and unaffected by rapid pacing from the high right atrium.

The authors feel that atrial flutter is generated by a focus of activity, which they define as possibly a very small area of tissue - ranging from a point source to circulation around a vena cava, but not involving all of the atrial tissue. Due to intervening atrial refractoriness, it may not be possible to affect such a small source of the tachycardia using rapid pacing. Although their criteria of morphology and beat-to-beat cycle length variation for these two forms of atrial flutter are identical, they still feel that the rhythms may be distinct separate entities, based on different response to rapid pacing, and also on the observation in two patients that "Type I" was converted into "Type II" using rapid pacing. In fact, what these two patients exhibited was no more than a change in atrial flutter rate on atrial stimulation, without a change in surface electrogram P-wave morphology. Such changes were frequent in the present study, and may or may not be accompanied by surface ECG changes (see Chapter 7). It is not necessary to invoke a new mechanism for a faster tachycardia, in order to explain lack of response to electrical stimulation, as this can be explained by virtue of the increased rate alone. Wells does not attempt to correlate his "Type II" flutter with the "uncommon" form of flutter already discussed, where surface ECG appearances are different. He notes, however, that uncommon flutter usually has a slower atrial rate - 250 beats per minute, or less - and has been referred to as "atrial tachysystole" (Puech, 1970),

implying that its mechanism is focal and distinct from that of the "common" form of flutter. Again, in the present study, in seven cases, atrial stimulation has converted the common form to the uncommon form, and vice versa, with minimal changes in cycle length (see Chapter 7). Any claims of differences in mechanism of these two forms of atrial flutter are not soundly based on experimental evidence. Wellens' group again presented evidence for a focal origin of flutter (Friedman, 1982). Two cases of common flutter were studied. It is of interest that single atrial extrastimuli, applied at various sites in the right atrium and coronary sinus, produced only local capture, followed by a fully compensatory pause. Distant atrial electrograms were unaffected. These findings are considerably at odds with those of the present study (see Chapter 5 and Chapter 7). One, two and three atrial extrastimuli were not able to terminate flutter. In one patient, atrial flutter could be maintained despite a 3:2 block between the coronary sinus and the high right atrium, and thus all of the atrial tissue was not required to sustain flutter. This finding is said to support a focal origin of flutter. In fact, it demonstrates only that inter- and intra-atrial dissociation can occur during atrial flutter, and does not exclude micro or even macro-reentry involving the considerable mass of atrial tissue not dissociated. Their observations that regular atrial activity is sometimes seen in one area, when atrial fibrillation is apparent elsewhere and on the surface ECG, could be said to support the theory of multiple small reentrant wavelets as the cause of atrial fibrillation (Moe, 1962; Allessie, 1985). Friedman states that the rhythm was not atrial fibrillation, because it was converted to sinus rhythm by a further burst of rapid atrial pacing. The tracing illustrated suggests, however, that pacing may not have affected the rhythm, which appears to spontaneously return to atrial flutter and then to sinus.

In summary, the evidence presented by various authors for a focal origin of atrial flutter is not conclusive. The type of flutter produced by focal administration of aconitine has not been shown to correlate with any clinical

arrhythmia, and the other main evidence is in the form of endocardial and epicardial mapping, with an inadequately small number of mapping positions to detail the spread of excitation.

2.3.3 Circus movement - the reentry concept

The fundamental basis of the circus movement theory is the absence of a point source as the origin of a tachycardia. Instead, this theory postulates that a wavefront continuously circulates around an obstacle, and the conditions of refractoriness, conduction velocity and pathway length are such as to maintain the circulating wavefront indefinitely. The first observations of circus movement in muscular tissue (Mayer, 1906) were made five years before atrial flutter was first described. Mayer cut off the sensory organs of a jellyfish, Cassiopea Xamachana, and observed that the tissue became paralysed. However, by cutting a hole in the centre of the disc, and then applying a momentary stimulus to the remaining ring, *"a rapid, rhythmical pulsation"* was set up, which in one specimen lasted for 11 days. It is obvious that some sort of unidirectional block must exist at the time of the initiating stimulus, otherwise waves would pass round the ring in both directions, and would be extinguished upon colliding. However, Mayer did not comment upon the need for this block. The initiating stimulus, and the condition of unidirectional block, are now considered to be two of the factors necessary for initiation of a circus rhythm (Allessie, 1977). The block is usually attributed to non-homogeneous refractory periods in the tissues surrounding the point of stimulation, and the stimulus must be applied at a critical time such that tissue in one direction may conduct, while in the other direction, tissue is refractory. The third condition held to be necessary is the existence of slowed conduction somewhere in the pathway, to allow the tissue ahead of the wavefront time to recover excitability (Allessie, 1977). Mayer made observations upon conduction velocity by performing a further elegant experiment. By means of a

complicated series of cuts, he doubled the length of the conduction pathway in the jellyfish ring. However, the conduction time around the circuit did not double, but increased only by 70%. This shows that the conduction velocity was increased by around 20% in the longer pathway, and Mayer postulated that this is due to

> *"the longer rest that the tissue enjoys, thus allowing it the more completely to recover and regain its sensibility to the stimulus which calls forth the contraction."*

Although conduction velocity in cardiac tissue does not alter during diastole, it has been shown that stimulation in the relative refractory period is associated with slowed conduction (Hoffman, 1960). This phenomenon explains Mayer's observations. One of the most important early papers on circus movement was written by G.R.Mines (Mines, 1913). His experiments on the tortoise heart, in which he set up "*circulating tachycardias*", led him to observe that circus movement is more likely to occur in the setting of slow conduction velocity, and short refractory period. He noted that ectopic beats could both initiate and terminate these arrhythmias, and went on to speculate that

> *"a circulating excitation of this type may be responsible for some cases of paroxysmal tachycardia as observed clinically."*

It has now been shown that some clinical arrhythmias are due to a reentry circus movement, for example atrio-ventricular tachycardia using an accessory conduction pathway (Wellens, 1975).

Sir Thomas Lewis carried out a series of experiments on atrial flutter in dogs (Lewis, 1920 (a)), involving direct epicardial measurements of activation times, using the surface electrocardiogram and a bipolar exploring electrode. He

suggested that in three animals in which atrial flutter was inducible by electrical stimulation, the activation wave seemed to circulate around one or both of the venae cavae. He showed that, at certain points in the atrium, the excitation wave travelled towards the initial site of stimulation. While suggestive of a reentrant phenomenon, this is not as conclusive as Rytand suggests (Rytand, 1966), because incessant local block close to the initial site cannot be ruled out. Lewis also observed that atrial activation occurred throughout the atrial flutter cycle, in contrast to sinus rhythm - again supportive rather than conclusive evidence of reentry. In 1947, Rosenblueth and Garcia Ramos developed a technique for reliable experimental induction of atrial flutter in the dog (Rosenblueth, 1947). They crushed part of the tissue between the venae cavae, thus preventing its excitation, and forcing a circulating wavefront to pass round both venae cavae rather than only one. In this model, flutter could be more reliably induced, and persisted for longer. Using this technique, several observers have tested the postulate that a circus rhythm should be terminated by division of the pathway at any point (Mines, 1913). Scherf (1928) and Blumenfeld (1960) failed to stop flutter by making cuts, and concluded that a focus existed. However, Rosenblueth (1947) and Kimura (1954) did succeed, and concluded that this experimental model of atrial flutter was a circus movement. Kimura's experiments involved the induction of both electrical and aconitine induced flutter, and he clearly showed by atrial mapping that, in aconitine flutter, excitation spread away from the point of administration of the aconitine, and occupied less than 30% of the flutter cycle length; in contrast, during electrically induced flutter, accompanied by the crush technique of Rosenblueth, excitation passed around the venae cavae, and occupied all of the flutter cycle. Katz (1959) and Rytand (1966) suggest that opposition to the above experimental evidence supporting circus movement may have been largely based on inappropriate experimental models of atrial flutter.

It would seem that the tachycardia induced by aconitine or delphinine satisfies the requirements of an ectopic focus, but it is very far from clear that such tachycardias have a relationship to clinically occurring atrial flutter. There have been numerous attempts (Lewis, 1920; Cabrera, 1947; Rosenblueth, 1947; Lanari, 1956; Kato, 1957; Hayden, 1967) to establish atrial activation patterns in atrial flutter by direct (epicardial) or semi-direct (oesophageal and anterior chest wall) recordings, but these, while suggestive of a circulating wavefront, are necessarily ambiguous and inconclusive, due to the small number of points recorded. Even with modern endocardial catheter recordings, and direct intra-cardiac measurements at open-heart surgery, usually less than 50 recordings can be made. The possible smallness of a reentry circuit, and the undoubted complexity of the excitation wavefront near the focus or circuit, means that probably several hundred recordings must be made. This has only been possible in experimental animals, and there is always the question of the relevance of animal experiments to clinically occurring atrial flutter in man. Despite this possible drawback, the experiments of Allessie (1973, 1976, 1977) and Boineau (1976, 1980) merit close attention. In Allessie's series of experiments, the left atrium of a rabbit was excised, and fixed in a tissue bath. The sino-atrial and atrio-ventricular nodes were carefully excised from the preparation, as was the part of the left atrium containing the entrances of the pulmonary veins. These steps ensured that no spontaneous activity existed in the specimen prior to stimulation. The finished specimen measured 15 x 20 mm. The stimulation was bipolar, via silver wires 0.5 mm apart, and consisted of a drive train of 20 stimuli, followed by an extrastimulus at increasing prematurity. Unipolar recordings were made via ten silver wires spaced 1 mm apart, mounted on a micro-manipulator. After recordings were made, the electrodes were moved, and the tachycardia re-initiated. In this way, up to 300 electrograms could be recorded from the preparation. To ensure that the spread of activation was always the same on different inductions of the arrhythmia, a fixed bipolar

reference electrode was used. This single reference was considered adequate by the authors, but is possibly not sufficient to ensure absolute reproducibility. Activation maps of the induced tachycardia were made. The duration of the tachycardia was variable, but usually short-lived. The cycle length started at around 50 ms, and increased to around 100 ms, leveling out after about 50 beats. Despite these variations in cycle length, the mapping showed that activation pattern was always continuous from one cycle to the next, and followed an apparently circuitous path, around an inexcitable area. The reason for the inexcitability of this area was investigated using a circular array of micro-electrodes, of variable diameter. It was clearly shown that, in the inexcitable area, the cells were being partially depolarised from opposite sides of the circuit. Because they were being stimulated twice as fast as the rest of the atrial mass, they were unable to respond with a full, propagated action potential, and instead only small, sub-threshold responses were seen. Thus these normal, viable cells were rendered effectively inexcitable by high rate stimulation, and an area of effective block was created. The possibility of terminating a circus movement tachycardia by making part of the functioning circuit refractory, even for only one cycle, must exist, but precise location of the delivered stimulus would, of course, be important. It is interesting to note that the dimensions of the circuit in Allessie's experiments are of the order of 5 x 5 mm, and the measured refractory period of the rabbit atrium is around 50-70 ms. In human atrial flutter, the cycle lengths are at least double those seen in these experiments, and the atrial refractory periods are 2-3 times longer. It would, however, be naive to extrapolate these comparisons to saying that the circuit in human atrial flutter is about 10 x 10 mm, since slowed conduction will play a large part in determining the circuit dimensions.

Allessie concludes by formulating the "leading circle" concept of circus movement tachycardia, in which no anatomical obstacle is required, and initiation depends on:

1) Non-uniform distribution of refractory periods

2) Slowed conduction

3) Critical timing and positioning of a premature beat.

The length of the circuit is said not to be dependent on anatomical factors, but to be functionally determined by the conduction velocity, refractory period, and stimulating efficacy. Consequently, there is said to be no excitable gap. However, this depends on the stimulating efficacy, so that a stimulus of greater efficacy than the circulating wavefront may be able to evoke a premature response (an "excitable gap"). This latter point has perhaps been misunderstood; it has sometimes been assumed that it is completely impossible to enter such a "leading circle" with a premature stimulus (Josephson, 1979). Since stimulation threshold rises in the relative refractory period, it is to be expected that premature beats can be provoked only by relatively high amplitude stimuli. Also of importance, and not stated by Allessie, is the possible non-uniformity of refractory periods in the actual leading circle. The cycle length will be determined by the **LONGEST** refractory period in the circuit, and consequently tissue with a shorter refractory period should exhibit a wider excitable gap. It is theoretically possible that a single stimulus applied to an area of short refractory period, but adjacent to an area of longer refractory period, and preceding it in the leading circle, might cause a premature beat, which blocked retrogradely with the leading circle wavefront, and blocked antegradely due to the longer refractory period. Tachycardia would then be extinguished. The difficulty in using such a method would be in trying to precisely locate a suitable stimulation site, and probably accounts for the low success rate in converting atrial flutter using single or paired extrastimuli (Wellens, 1978), as previously described, and see Chapter 6.

Boineau (1976) studied atrial flutter occurring spontaneously in a dog without heart disease. The dog exhibited two forms of atrial flutter, with different surface electrocardiographic appearances. The Type 1 flutter had a similar appearance to common atrial flutter in man, and Type 2 resembled atypical (uncommon) flutter. Intra cardiac mapping revealed an area of slow conduction, which was caused by *"hypoplasia and abnormal atrial muscle band continuity"*. A total of 96 bipolar epicardial electrograms were recorded, and it was shown that, during both types of flutter, slowed conduction allowed reentry to occur. In Type 1 flutter, the circuit moved clockwise around the superior vena cava (viewing the atria from the BACK). In Type 2 flutter, the rotation again was around the superior vena cava, but was anti-clockwise. A very interesting finding was made during Type 2 flutter, which, like atypical flutter in man, exhibited more discrete P-waves on the surface electrocardiogram. The isoelectric interval on the surface trace did not correspond with a lack of atrial activity. Instead, activation was proceeding in a closed circle, and the resultant electrical vector was zero. Only when the wavefront was blocked by an atrial wall or a refractory area, did a resultant electrical vector appear in the surface leads. It should therefore be borne in mind that it is dangerous to infer too much about precise intracardiac activity, and particularly its absence, from surface electrograms. Boineau proposes that the basic cardiac abnormality underlying atrial flutter is an abnormal impulse propagation, due to hypoplasia or discontinuity of muscle bands, which could be congenital or acquired (Boineau, 1980). Such a condition would not become apparent until the dynamic factors of non-uniform refractoriness and critically timed and placed premature beat combined to initiate the arrhythmia.

Pastelin (1978) performed an interesting study on atrial flutter in dogs, implicating the specialised atrial conduction pathways in flutter. It was pointed out that atrial myocardium cannot be considered to be a homogeneous

conducting system, and they suggest that the inter-atrial band (Bachmann's bundle) may have an important part to play. Left atrial ectopic impulses may be rapidly conducted along Bachmann's bundle to its junction with the anterior internodal tract, where asymmetric conduction, with uni-directional block, might occur. They suggest that flutter can be maintained solely by a circulating impulse in these specialised tissues, and reinforce this argument by showing persistence of flutter in the special pathways in the presence of elevated serum potassium, despite simultaneous absence of activity in normal atrial myocardium. Another interesting observation in this paper was the finding of equal frequencies of flutter before and after applying the crush technique (Rosenblueth, 1947) to the area between the venae cavae. The implication is that block in this area is not vital to the occurrence of flutter, as has often been stated in papers using the crush technique.

Inoue studied atrial extrastimulation in human beings during spontaneous atrial flutter (Inoue, 1981). An excitable gap was found to exist, and subsequent flutter cycles could be advanced (reset). The excitable gap varied from 14% to 25% of the flutter cycle. Peripheral left atrial stimuli were followed by fully compensatory pauses, said to indicate non-involvement in the mechanism supporting flutter, but high and low right atrial stimuli produced return cycles equal to the basic cycle length, suggesting that these sites were involved in a macro-reentry circuit. Inoue places great emphasis on the fact that some stimuli caused shortening of the next cycle rather than the cycle containing the impulse; however, this is simply due to the fact that he was recording at a remote position from his stimulation site, e.g. stimulating high right atrium, and recording from an oesophageal lead. This finding does not conclusively verify the existence of reentry rather than an ectopic focus, as will be discussed in Chapter 5.

Plumb, James and Waldo considered the effects upon atrial flutter of rapid atrial pacing. It was repeatedly the case in their series that the rate of the

flutter could be increased by rapid stimulation, without interrupting the flutter (Plumb, 1980). This was explained by postulating repeated early anterograde (orthodromic) entry into a circuit, with retrograde (antidromic) block of the paced and spontaneous impulses. More rapid atrial pacing causes this collision to occur earlier in the loop, and atrial fusion can be demonstrated in intra-atrial electrograms. In another paper, the same group (Waldo, 1977) showed that this "entrainment" of flutter without interruption did not alter the surface electrograms. Only when the rate was critically rapid did the surface P-wave become positive in leads II and III. This occurrence was associated with termination of flutter, as the reentry circuit had presumably been abolished, and the artificial pacemaker was in complete control of the heart. The critical point in this paper is the demonstration that high right atrial pacing above the flutter rate can give rise to negative P-waves in leads II and III during entrainment, although pacing from that site would normally give positive P-waves in these leads. It is very difficult to find a convincing argument to explain this phenomenon on the basis of a low atrial ectopic focus, and only macro-reentry offers an adequate explanation.

Perhaps the most thorough electrophysiological investigation of atrial flutter in man was carried out by Disertori (1983). Thirteen patients with spontaneously occurring atrial flutter of the common form were studied. Two or three quadripolar catheters were inserted, giving recording and stimulation from low septal right atrium (or coronary sinus) and high right atrium, in all patients. In 5 patients, recordings were also made from the low or mid lateral right atrial wall. In all patients, low septal activation preceded activation of the high right atrium. Single stimuli were given to the high right atrium, and the subsequent cycles were reset (no compensatory pause was noted). Although high right atrial activation followed low septal, reset caused by high atrial stimulation was followed by reset of the next low septal cycle - suggesting entry into a circuit. Double and triple high atrial stimuli caused conversion of rhythm in

10 patients; in 3, sinus rhythm was restored following one last, spontaneous flutter beat - this finding is mirrored in the present study (see Chapter 5). In 6 patients, several seconds or minutes of atrial fibrillation preceded the restoration of sinus rhythm, and in the remaining patient, a faster flutter was induced, which was self-terminating after 25 seconds. Three patients were not converted. This study represents by far the highest success rate in conversion of atrial flutter by conventional programmed stimulation, with 39% success rate for 2 stimuli, and 77% for three stimuli. Several criticisms of the accuracy and relevance of the precise measurements have to be made, however.

1) The fixed, non constant current stimulus strength of 10 Volts does not allow comparative measurements of effective refractory periods or excitable gaps to be made between the different atrial sites or patients in the series, since it is well known that refractory periods are shorter at higher relative stimulus strength (Josephson, 1979). Stimulus strengths should always be referred to diastolic threshold in order to allow inter-patient and inter-series comparisons to be made.

2) Some of the records were taken at a paper recording speed of 50 mm/s; this is probably not fast enough to make sufficiently accurate measurements (Josephson, 1979; Wellens, 1980).

3) No mention is made of the criteria used to determine the point of activation from a bipolar electrogram; Wellens (1980) suggests that the local activation time is represented by "*the peak of the bipolar electrogram*". This statement needs to be modified when recording during atrial flutter. Due to slowed conduction, the bipolar electrogram can sometimes resemble two unipolar

electrograms of opposite polarity; and, unless contact is the same at both electrodes, the bipolar signal will look more like a unipolar signal, to a degree determined by the relative contact (see Chapter 4, section 4.5).

Accordingly, it is essential to recognise these variables and define measurement criteria, which Disertori does not mention. For instance, by the criteria used in this study, Disertori's Figure 1 shows stimulation of the high right atrium, with a flutter cycle length of 250 ms, a refractory period of 200 ms, and a return cycle of 250 ms - a non-compensatory pause. The text states that the refractory period is 180 ms, and return cycle is 270 ms.

A recent paper on the subject describes further experiments carried out by Allessie's group (Allessie, 1984). Atrial flutter was induced in isolated, perfused dog hearts by infusion of acetylcholine and rapid pacing, and the intact atria were mapped using egg-shaped electrodes inside each atrium; each egg contained 480 contacts. Up to 960 electrograms could be recorded (in 5 banks of 192 simultaneous electrograms). The results extend and confirm their own findings in rabbit atria (Allessie, 1973, 1976, 1977); reentry can occur in normal tissue without an anatomical obstacle. They found that the circuit in their cases of induced atrial flutter could be anywhere in either atrium. Although atrial activation is continuous, the amount of atrial tissue depolarising at any given time is highly periodic, varying from 20% to less than 1%; Allessie suggests that this will be responsible for an undulating, sawtooth like surface ECG pattern no matter where the circuit lies. Spontaneous termination sometimes occurred due to development of a conduction delay in the circuit, but sometimes an abrupt block occurred without previous slowing. As with rabbit atria, a functional block was created in normal tissue; depression of excitability resulted from partial depolarisation twice in every cycle from opposite sides of the circulating wavefront. Allessie

concludes that this type of atrial reentry with minimal excitable gap may be responsible for the faster rates of atrial flutter seen in man, and slower varieties may also include an anatomical obstacle inside the pathway; these will be slower, more stable, and will show a larger excitable gap.

Cosio described endocardial mapping in 13 cases of flutter (Cosio, 1986), and found areas of split or fragmented activation (duration at least 90 ms) in all patients, usually located on the posteroseptal right atrium. Thirty-four of 178 electrograms (19%) were split or fragmented. A circus-like movement of activation was inferred in most patients, with most of the split electrograms said to be in the postulated reentry circuit. One problem with this interpretation is the postulated reentry circuit, which in this study is usually composed of 3-5 electrograms from adjacent sites. The inference of reentry from this number of sites is, at best, arguable, and the opportunity to confirm reentry using multiple site programmed stimulation, as in the present study, was not taken.

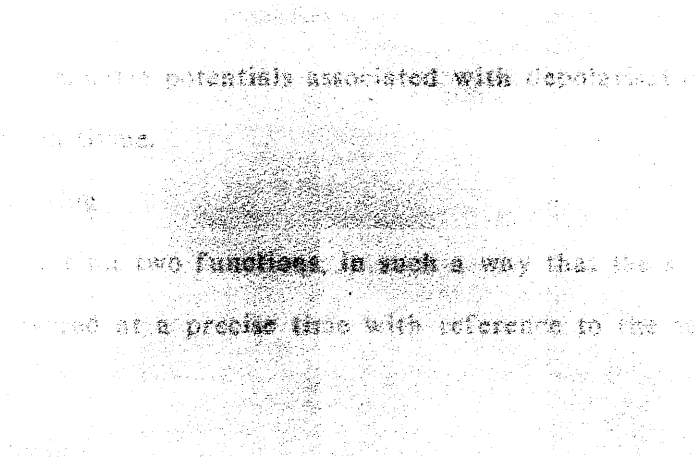
In summary, it appears that the great bulk of evidence from in vivo and in vitro animal studies points to a reentrant mechanism being responsible for clinically occurring atrial flutter. There is, however, a lack of convincing non-circumstantial evidence of the true mechanism of human atrial flutter, due to the difficulties in its investigation in the intact or surgically opened beating heart, and this has led to somewhat subjective interpretation of such clinical data as can be obtained. Attempts have been made to explain the mechanism of flutter using mapping or stimulation, but the two techniques have not been fully exploited in combination.

2.4 Aims of the present study

The present study will attempt to further elucidate the mechanisms underlying spontaneously occurring atrial flutter in man, by the use of multiple site atrial mapping, closely combined with electrical stimulation and observation of

resulting activation patterns and intervals. Particular attention will be paid to areas exhibiting a reset response to atrial stimulation (non-compensatory post-stimulus cycle). Refractory periods will be measured at multiple sites, to investigate the presence or absence of inhomogeneity, and areas of apparent slow conduction will be investigated; these are two of the three criteria stated above for creation of a reentry tachycardia.

A new method of stimulation will be used to attempt conversion of atrial flutter. The method, termed "Atrioversion", will use a constant current stimulus of pulse width greater than the flutter cycle length, and delivered at a site as close as possible to the origin of the flutter (as determined by mapping and stimulation), the hypothesis being that disruption of the flutter activation pattern by the long stimulus may terminate flutter.



Chapter 3

THE DEVELOPMENT OF THE ATRIOVERTER

3.1 Introduction

The original circuitry used in the Atrioverter was designed and built by the author in the Western Infirmary, Glasgow. Subsequently, in order to expand the system to include multiple amplifiers, a new system was designed by the author and developed in the Electronics Labs of the Department of Clinical Physics, Glasgow.

The display elements of the system were an 8 channel Hewlett Packard monitor, a Siemens Elema Mingo 82 inkjet recorder, and a Racal 7 channel FM tape recorder.

In common with most physiological stimulating systems, the Atrioverter has four main functions to carry out. These are :

1) Stimulation

Deliver one or more stimuli at precise amplitude and pulse width.

2) Sensing

Amplify the electric potentials associated with depolarisation of the stimulated tissue.

3) Synchronising

Interface the first two functions, in such a way that the stimuli can be delivered at a precise time with reference to the sensed potentials.

4) Shock logic

Trigger the stimulating circuit after preset delay or combination of delays, activated by signals from the synchroniser unit.

3.2 The stimulating circuit

The concept of atrial cardioversion (Atrioversion) was first developed in 1978 as a low energy form of Cardioversion, in which a stimulus would be delivered to the atria via an electrode catheter. By delivering the energy directly to the abnormal tissue, it was hoped that lower energies could be used to effect conversion. In the first Atrioverter design, in 1979, the stimulus had an identical form to the "Lown" waveform used in defibrillators (a similar system, using a truncated exponential waveform, was described as an implantable cardioversion device (Zipes, 1982)) . A 16 uF capacitor was charged up to a variable voltage (up to 500 Volts), and discharged into the patient through a series 40 mH inductor (see Figure 3.1). The maximum stored energy was 2 Joules. The component values were chosen to be identical to the defibrillators in use in the Coronary Care Unit of the Western Infirmary, Glasgow in 1979. Most defibrillators now use a 32 uF storage capacitor, allowing a lower stored voltage to deliver the same energy (according to [Energy]= 0.5 x [Capacitance] x $[Voltage]^2$). The series inductor modifies the rise time of the waveform, which takes on the shape of an underdamped sine wave, decaying to zero in less than 10 ms if the patient impedance is low (see Figure 3.2).

The equation for the shape of the pulse is :

$$V = V_0 A e^{-kt} . \sin(n't)$$

where:

Vo= stored voltage	C = capacitance
A = constant = R/n'L	k = damping factor = R/2L
R = patient resistance	$n' = (1/(LC) - k^2)^{0.5}$
L = series inductance	t = time

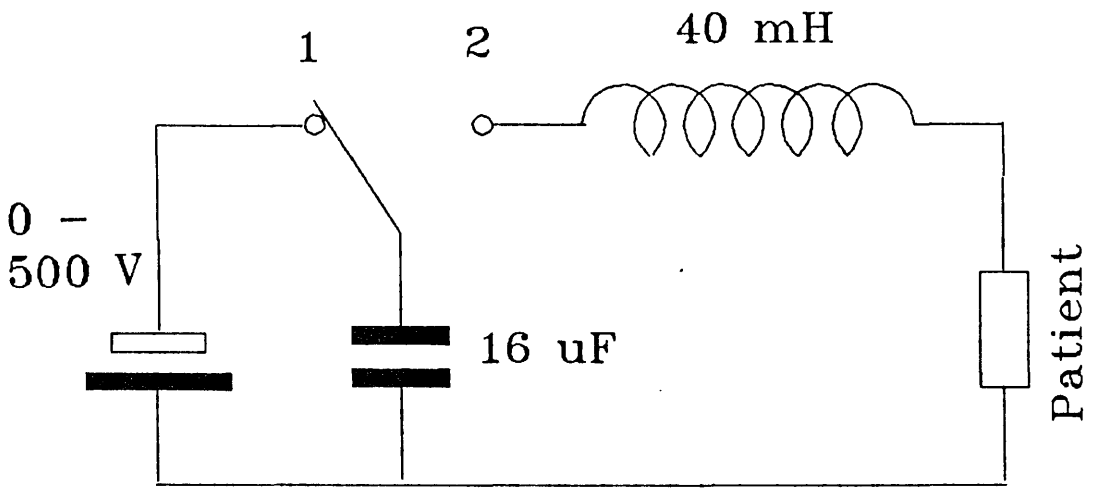


Figure 3.1

The output circuit of the Mark I Atrioverter.
When the switch is in position 1, the capacitor is charged to a variable voltage (0–7kV). When the switch is in position 2, the capacitor is discharged into the patient through the series inductance.

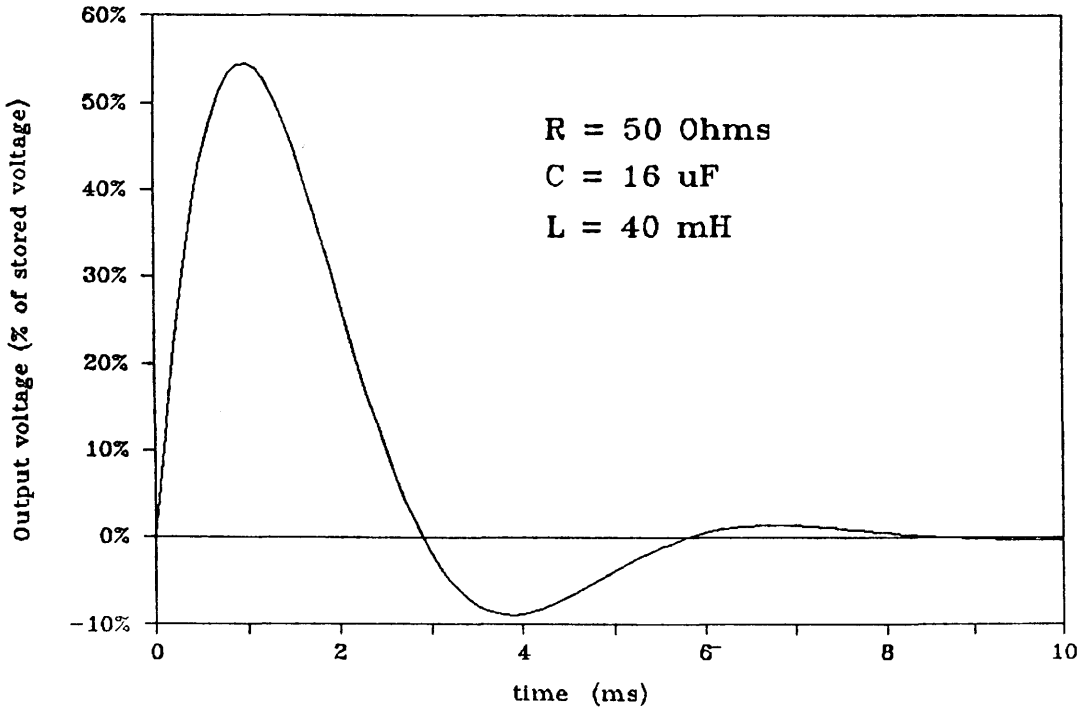


Figure 3.2

Output waveform of Mark I Atrioverter for a 50 Ohm resistive load. The underdamped sine wave trace decays to zero in less than 10 ms.

This pulse shape is illustrated in Figure 3.2. Figure 3.3 shows an oscilloscope trace depicting the relationship between a surface electrogram with superimposed sync marker, and a delivered shock.

It can be seen that n' is a real number only if:

$$k^2 < 1/(LC)$$

$$\text{hence } R^2/(4L^2) < 1/(LC)$$

$$\text{or } R^2 < 4L/C$$

If R exceeds the critical value $(4L/C)^{0.5}$, then the output pulse will no longer be an underdamped sine wave, but will follow the usual exponential capacitor discharge curve, with rise time and downslope time constant increased only slightly by the series inductor. With the values of L and C used in the first Atrioverter, the critical value of R is 100 Ohms. Hence, if R is greater than 100 Ohms, the series inductor will have little or no effect, and a relatively high peak current will be delivered immediately at the start of the pulse.

An experiment was carried out to estimate the typical resistance to be encountered by the pulse. Atrioverter pulses of between 10mJ and 1J were delivered to whole blood. Current and voltage were measured directly on an oscilloscope. The measured resistances varied between 300 and 450 Ohms. These values agree approximately with intracardiac resistances obtained during permanent pacing. At the lower voltages involved in permanent pacing, resistance varies between 300 and 1000 Ohms. The very high voltages during defibrillation presumably cause electrolytic changes in the tissue which account for the low (approximately 50-75 Ohms) resistance found. In addition, the small surface area of an intracardiac electrode will result in a higher impedance than with large defibrillator paddles.

It follows from these results that the pulse delivered by the first Atrioverter stimulating system will not be a "Lown" pulse, but will be a decaying exponential capacitor discharge.

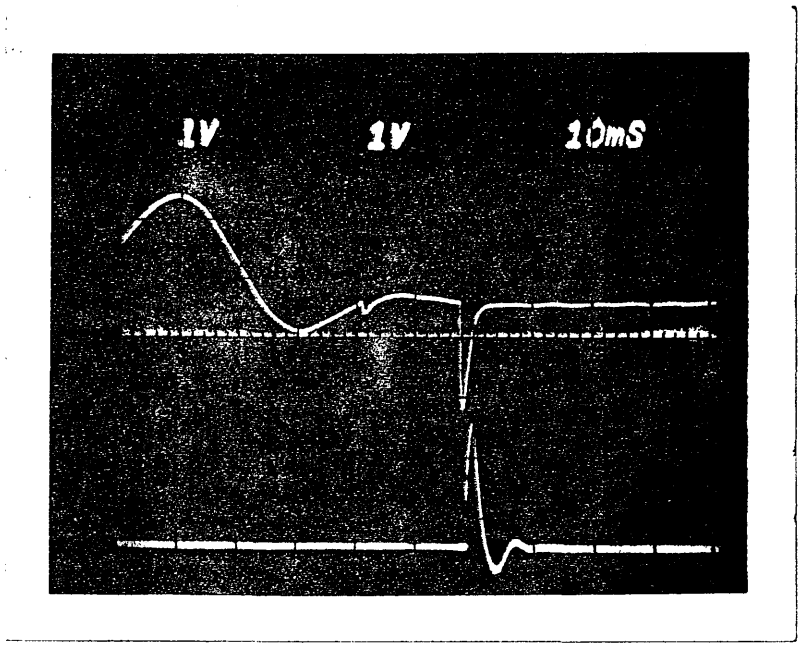


Figure 3.3

The output pulse of the Mark I Atrioverter (lower trace) is delivered at a set delay from the peak of the sensed electrogram (upper trace), which has a marker superimposed to show the timing of the shock.

The initial circuit design was abandoned after demonstration that effective conversion could not be achieved with energy levels below the pain threshold (approximately 50 - 100 mJ). The shock was delivered through a bipolar catheter placed in the lateral right atrium. In five patients (2 with atrial flutter, 3 with atrial fibrillation), only one rhythm conversion was achieved, when a flutter was converted to atrial fibrillation, apparently due to stimulation during the atrial "vulnerable" phase. It was decided that low energy conversion of atrial flutter must be achieved in a more subtle manner.

The concept of the current Atrioverter was that an atrial stimulation site could be depolarised by a stimulus, and then held in a refractory state by a very long duration impulse. If the impulse was longer than the cycle length of the tachycardia, then the stimulation site would be inexcitable during the next tachycardia cycle. If, in addition, that site was essential for maintenance of the arrhythmia (eg it formed part of a reentry circuit), then the tachycardia would be terminated. Accordingly, the impulse should be constant current, and have a duration which could be set to greater than the atrial flutter cycle length.

The stimulating circuit used an open collector output (see Figure 3.4) connected to the patient through a coupling capacitor. This capacitor ensures minimal damage to the patient in the event of component failure. The circuit operation is as follows. The output transistor, Tr3, is normally off, preventing current flow, because its base is held at -80 V by Tr2, which is also normally off, and is in turn held that way by Tr1. When the base voltage of Tr1 exceeds -1 V due to the presence of the "shock trigger" pulse, Tr1 switches on, and its collector voltage will become -0.3 V. Tr2 is an emitter follower, whose emitter voltage will now be -1.0 V, and thus 79 V will be placed across the potential divider R2 and VR1. Depending on the position of the wiper of VR1, a variable base voltage will be placed on Tr3. This will set the emitter voltage, and thus the emitter current through the fixed resistor R3. The collector

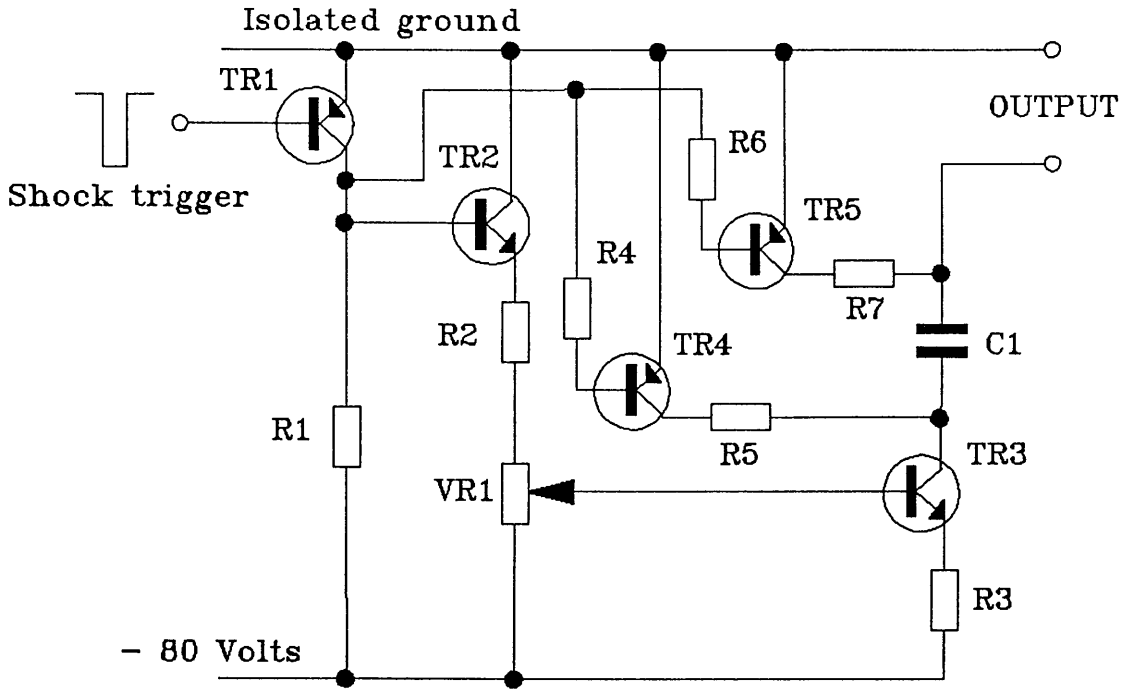


Figure 3.4

The output circuit of the Mark II Atrioverter (see text).

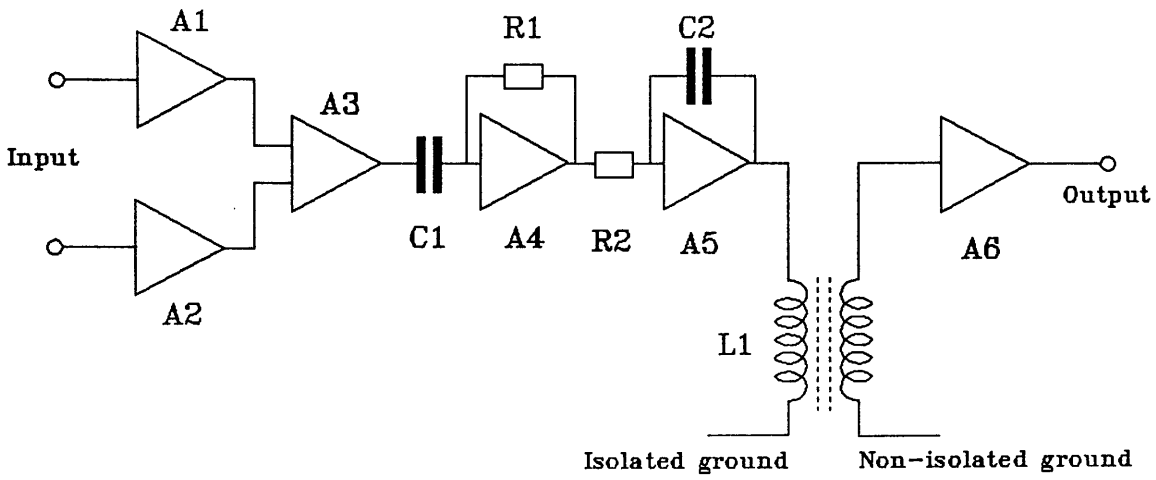


Figure 3.5

Schematic diagram of the sensing amplifier (see text).

current of Tr3, which is the output current will be identical to the emitter current unless it exceeds 80 Volts / (Rpat+R3), where Rpat is the effective patient resistance. From experience of permanent pacing, this is unlikely to exceed 1000 Ohms. The 80 Volt power supply allows the maximum 50 mA output to be delivered even if Rpat is 1500 Ohms.

When the shock trigger ends, Tr1, Tr2 and Tr3 all switch off, and the output current ceases. To expedite discharge of the coupling capacitor, C1, Tr4 and Tr5 then are switched on, and discharge C1 to ground through small value resistors R5 and R7.

The coupling capacitor was of a particularly large value, to allow for the long pulse widths, and to avoid " drooping " of the tail of the pulse (ie a fall-off in amplitude) at low levels of patient impedance and long pulse widths. The specification decided upon was :

> A pulse of 500 ms pulse width delivered into a 500 Ohm patient impedance shall not drop in amplitude by more than 10 %.

This specification was decided upon on the basis that the maximum pulse width likely to be required would not exceed 500 ms, and that drop in amplitude of 10% would not significantly alter any constant current, effect, since the shocks would always be delivered at a minimum of twice the stimulation threshold, as is conventional (Josephson, 1979).

The pulse shape is given by the usual equation,

$$V = V_0 e^{-t/RC}$$

where:

V = voltage

V_0= initial voltage at t=0

t = time

R = patient impedance

C = capacitance

Using the specification, V/Vo = 0.9 when R=500 Ohms and t=500 ms, a value of C = 10,000 uF is obtained. This very large value of C has associated problems. The stimulating system is also used to deliver conventional exploratory shocks to the heart, with a pulse width of 2 ms. When these short pulses are being used in the overdrive pacing mode, impulses may be delivered at up to 400 per minute, for several minutes. In the interval between stimuli, the capacitor must be discharged, otherwise it will eventually charge up to the power supply voltage (-80 Volts), and the output amplitude will decline to zero. As previously stated, two transistors are connected to each end of the capacitor to effect rapid discharge of the capacitor during the off-time, without sending the current through the patient.

The stimulator is calibrated in milli-Amperes, from 0 to 50 mA, continuously variable. To ensure full amplitude with high impedance loads, a high-voltage supply must be used. As stated above, the stimulator will deliver its full 50 mA into any patient impedance less than 1500 Ohms, due to the 80 Volt power supply, from high energy alkaline batteries (Mallory Duracell). In practice, it is rare to use as high a current as 50 mA, and patient impedance is usually under 1000 Ohms.

3.3 The sensing circuit

Bipolar intra-atrial signals have an amplitude of between 0.5 and 5 mV when the electrode is in contact with the atrial wall. The sensing circuit is shown schematically in Figure 3.5. A1 and A2 act as high input impedance buffers to the bipolar input signal. A3 differentially amplifies the signal with minimal gain but very high common mode rejection ratio, to eliminate mains-frequency interference. A4 is a schematic of the high pass filter stage, whose cut off frequency is variable between DC and 500 Hz. The filter is actually second order linear phase. A5 shows the low pass filter (which is again 2nd order linear phase). Its cutoff value is variable between 20 and 10,000 Hz.

Both of the filter stages also amplify the signal, which at the output of A5 has been amplified by x100 for an overall gain of 1,000. The signal is then passed to an isolating transformer L1 (in the later versions of these amplifiers, opto-isolators were used). The final stage amplifier A6 introduces 20 dB gain to produce the non-isolated output. The overall gain is selectable between 10 and 10,000. In addition, calibration pulses representing 1 mV may be displayed.

It is common to use a gain of 1000 and a bandwidth of 50 to 500 Hz in order to amplify intra-cardiac signals. In practice, atrial signals during flutter can be slow-moving and of lower amplitude, so variable gain and bandwidth were important. The system is fully patient isolated. Initially, power was supplied by high capacity batteries, and subsequently the power supplies were mains powered with full isolation.

3.4 The synchroniser unit

An electrogram, usually intra-cardiac, is selected for synchronisation of the output stimuli. It is preferable to choose an electrogram from as close as possible to the stimulation site. In practice, this usually means recording the electrogram from two electrodes of a quadripolar catheter, and stimulating

through the other two electrodes. The synchroniser (Figure 3.6) has an automatic gain control on the input amplifier (A1), which differentiates the signal from the sensing amplifier output, with a -3 dB point of 30 Hz. This signal is full-wave rectified (A2), The signal is then passed to a voltage comparator (A3), which outputs a marker logic pulse each time the signal exceeds a reference voltage (Vref). The output pulse width is 50 ms, and further triggering is prevented during this period.

The marker pulse is used to trigger the shock logic circuit (see below), and can also be superimposed on the electrogram, showing the point in the flutter cycle at which any stimulus will begin.

3.5 Shock logic

It is normal to deliver only single stimuli during an Atrioversion procedure, but to allow preset delays to be used, and to allow more complex electrophysiological protocols to be evaluated and compared with Atrioversion, a logic unit is used (Figure 3.7) to trigger the shock. It is in turn triggered by the marker pulse from the synchroniser unit. In the following discussion, the positive power supply (Vcc) will be referred to as "high", and the ground state as "low", in accordance with normal practice for binary logic circuits.

The circuit is composed of a delay generator, passive circuitry, and three "NAND" gates, each of whose output will always be high unless all of the inputs to that gate are simultaneously high, when the output goes low.

The "sync" output pulse is input to a delay generator, which outputs a high pulse a preset time (0-999 ms) after each sync pulse. This output is fed to one of the inputs of the triple-NAND gate (N3). The second input is sent high only when the "fire" button is pressed, and the third input to N3 is controlled by the "disable" latch (gates N1 and N2). At switch on, R3 pulls the output of N1 low and forces the output of N2 high. This situation remains stable, thus effectively preventing an output from N3, which requires all three inputs to be

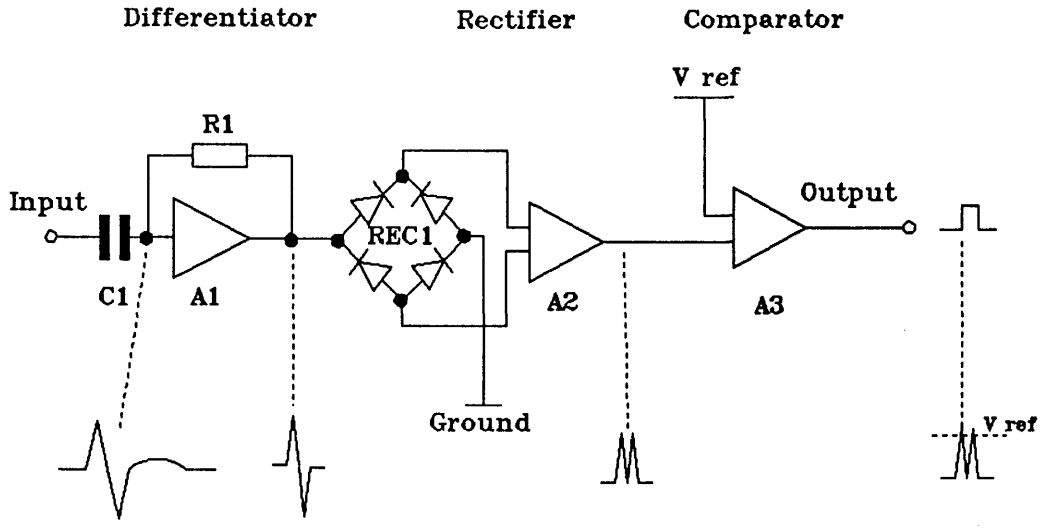


Figure 3.6

Schematic diagram of synchroniser circuit, showing waveform at various stages of circuit.

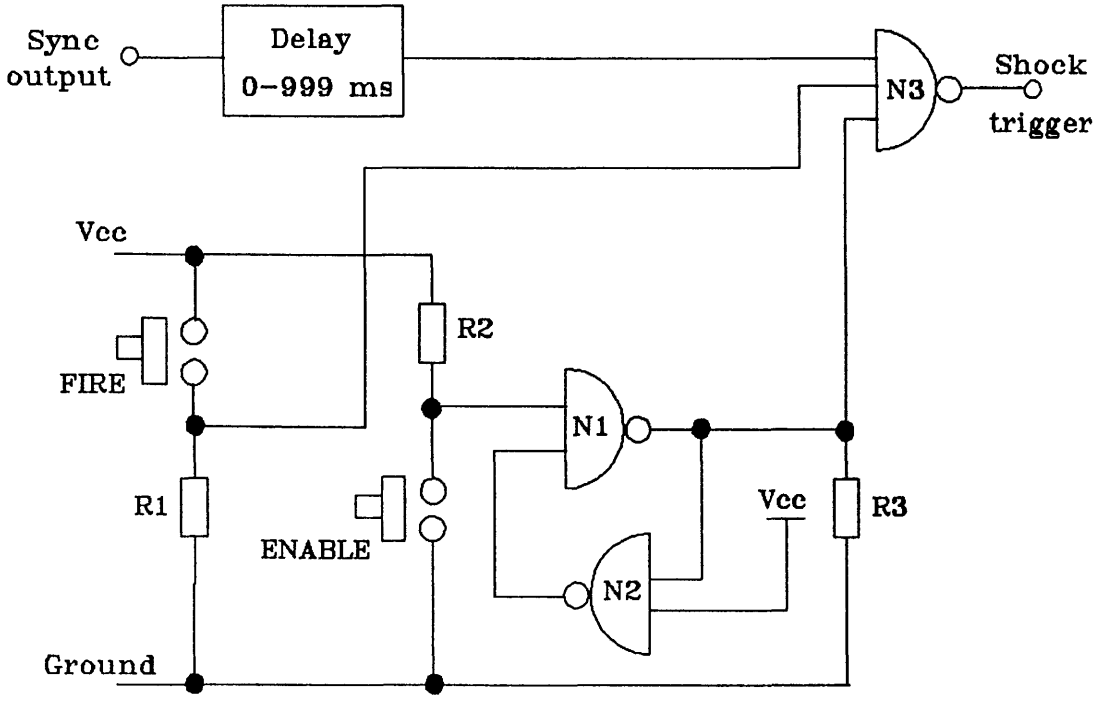


Figure 3.7

Simplified logic diagram of output trigger circuit ("shock logic")

high before its output can change state (producing the "shock trigger" pulse). When the "enable" button is pressed, the output of N1 immediately goes high, and the output of N2 then goes low, which latches these two gates in this new ("enabled") state. A shock trigger pulse will now be produced when a delay pulse arrives at N3 and the FIRE button is being depressed simultaneously. A pulse generator, not shown, regulates the output pulse width (variable between 0.1 and 999 ms), and also resets the latch to the "disabled" state at the end of the output pulse.

Further standard circuitry (not shown) allows one, two or three stimuli to be given at coupled delays selectable from 1 to 999 ms, with an accuracy of 1 ms. In addition, rapid pacing may be performed at rates of up to 1000 stimuli per minute. This system has been expanded to allow full electrophysiological studies to be carried out, but it should be borne in mind that, initially, the procedure was carried out using one intra-cardiac signal and one surface lead. Any additional recorded signals increase the information derived from an Atrioversion study, but are not an essential part of it. Figure 3.8 shows recordings made during atrial flutter in an early patient in the series. The intra-cardiac trace clearly shows atrial depolarisations, occurring at a rate of 285 per minute. The high pass filter was set at 10 Hz, allowing clear visualisation of the atrial repolarisation wave, the T_a wave. Parenthetically, it is interesting to note that atrial repolarisation does not occupy the full atrial flutter cycle (see discussion in Chapter 2 on the experiments of Allessie), and there is therefore presumably an excitable gap following full repolarisation. Atrial stimulation confirms that this is the case (see Chapters 5,6 and 7).

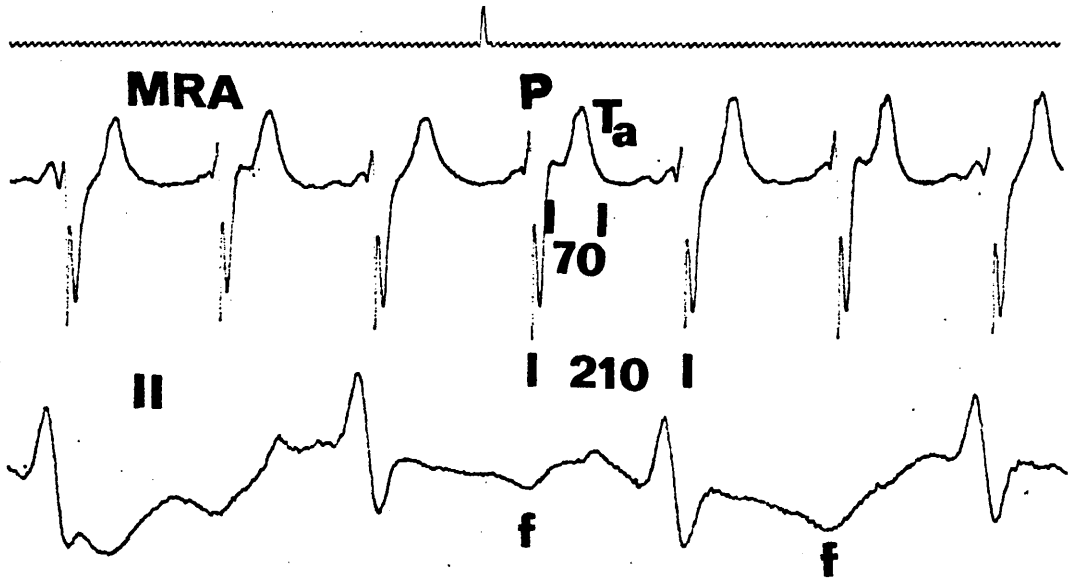


Figure 3.8

A mid right atrial electrogram (MRA) and surface lead II during flutter. The cycle length is 210 ms. The MRA electrogram shows a distinct atrial T wave ("Ta") of duration 70 ms. The total P-Ta duration is 120 ms.

Chapter 4

ELECTROGRAM RECORDING AND ATRIOVERSION PROCEDURE

This chapter will discuss the procedure by which Atrioversion is carried out, and will also look at theoretical aspects of electrogram recording and applications of this theory to practical interpretation of electrograms.

The current Atrioversion procedure is divided into four stages, namely:

1) Patient presentation and diagnosis
2) Catheterisation
3) Electrophysiological investigation of arrhythmia
4) Electrical conversion of arrhythmia

4.1 Patient presentation and diagnosis

Patients who undergo Atrioversion most frequently present as symptomatic hospital admissions to the Accident/Emergency department, or develop a tachycardia during a hospital admission. The most common symptoms of these tachycardias are shortness of breath, dizziness and chest pain or discomfort. Less frequently, patients are unaware of their tachycardia, and are identified by routine ECG at an out-patient clinic visit, or are referred by their general practitioner. This latter group of patients tend to have slower tachycardia rates and hence are asymptomatic or considerably less symptomatic. Because of this, they have often tolerated the tachycardia for a longer period, often several months. The time since onset of tachycardia is a significant factor in determining the success of attempted conversion (see Chapters 2, 5 and 6). When a patient is highly symptomatic, an intravenous injection of an anti-arrhythmic agent, such as verapamil or practolol, will often have been given in the emergency room. Some 20% of patients in the Atrioversion series fall into this category (see Chapter 5 and Chapter 6). These patients are, in a sense, a

different subgroup of the total population presenting with that arrhythmia; they are, to a greater or lesser extent, drug-resistant. It is debatable, however, whether the sensitivity of a tachycardia to electrical conversion is affected by resistance to drug conversion. The emergency patients are admitted to the Coronary Care Unit of this hospital, and the less urgent cases to the Cardiac Investigation Ward. A full 12-lead scalar electrocardiogram is recorded, and carefully analysed for evidence of rapid, organised atrial beating, with or without partial atrio-ventricular block. Atrioversion is attempted if the rhythm is seen to be atrial flutter.

The atrial rate in atrial flutter is usually between 280 and 320 beats per minute, although it may be as low as 200 beats per minute in rare cases (lower rates than 200 would normally be classed as atrial tachycardia), and can approach 400 beats per minute. The lower rates are usually due to drug therapy which slows but does not terminate the flutter (commonly chronic amiodarone therapy), but rarely a slow flutter may be seen in a patient with congenital malformations of the atria (Braunwald, 1980).

The ventricular response to this rapid atrial rate is variable, but in an untreated patient, an undiseased A-V node will usually give a 2:1 response, resulting in a ventricular rate of around 150 beats per minute. The common appearance on the surface electrocardiogram is to find large negative flutter waves in leads II,III and aVF, which continuously undulate throughout the cardiac cycle (the characteristic "sawtooth" pattern). The P-waves are usually relatively flat in lead I, and often discrete positive or biphasic P-waves are seen in the anterior chest leads. Figure 4.1 shows a surface ECG tracing from a patient with the common type of atrial flutter. Less commonly, positive flutter waves are seen in leads I,II or III. This uncommon pattern of flutter (see Figure 4.2) accounts for less than 10% of clinically occurring cases of atrial flutter in man, and some authors have postulated that its mechanism is different from the so-called common flutter described above.

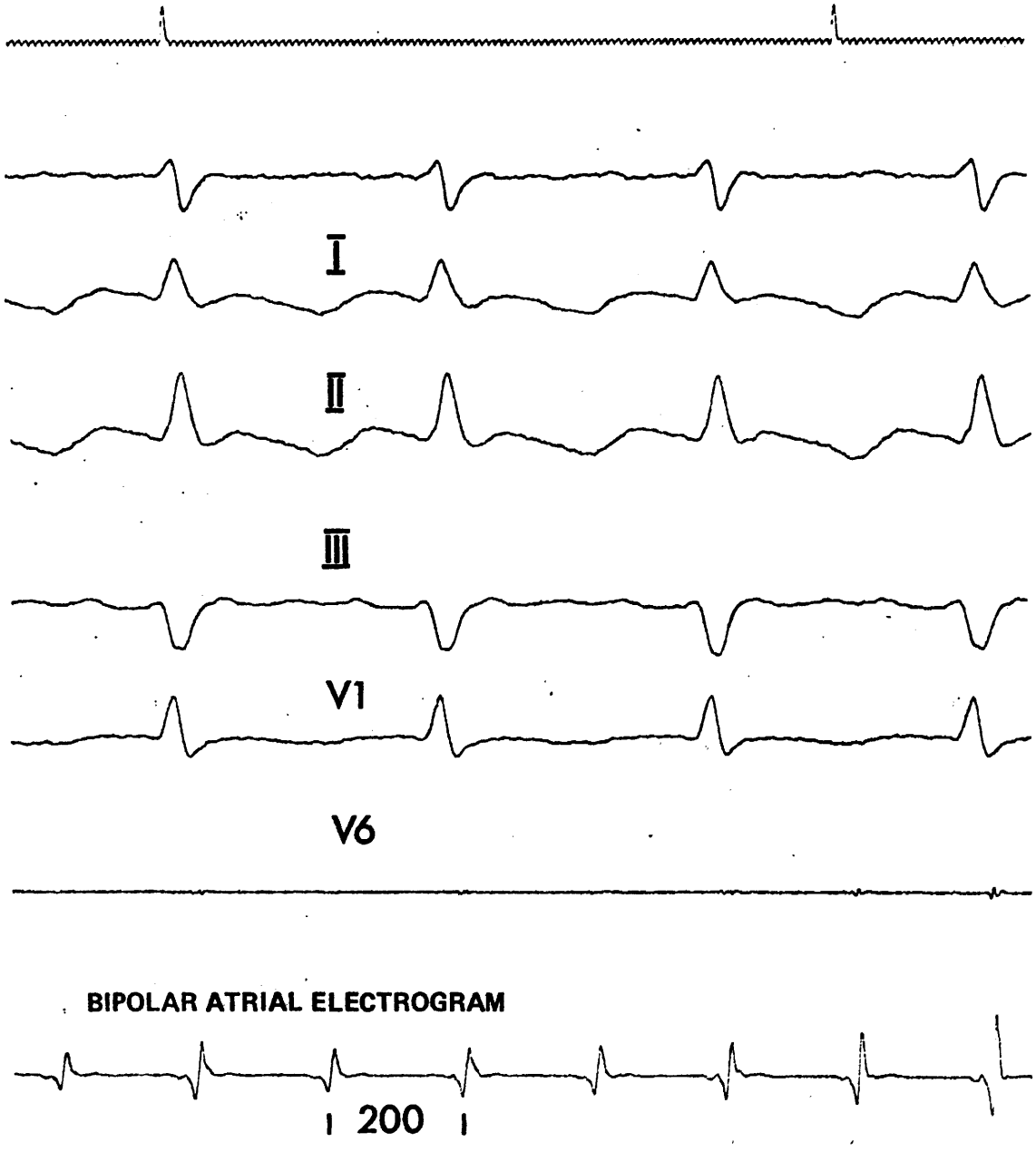


Figure 4.1

The common form of atrial flutter. Surface leads I, II, III, V1 and V6 show atrial flutter with 2:1 A-V block. A bipolar atrial electrogram confirms that the atrial cycle length is 200 ms (atrial rate 300 bpm). In this and all other traces, the top line shows time markers at 1 second intervals.

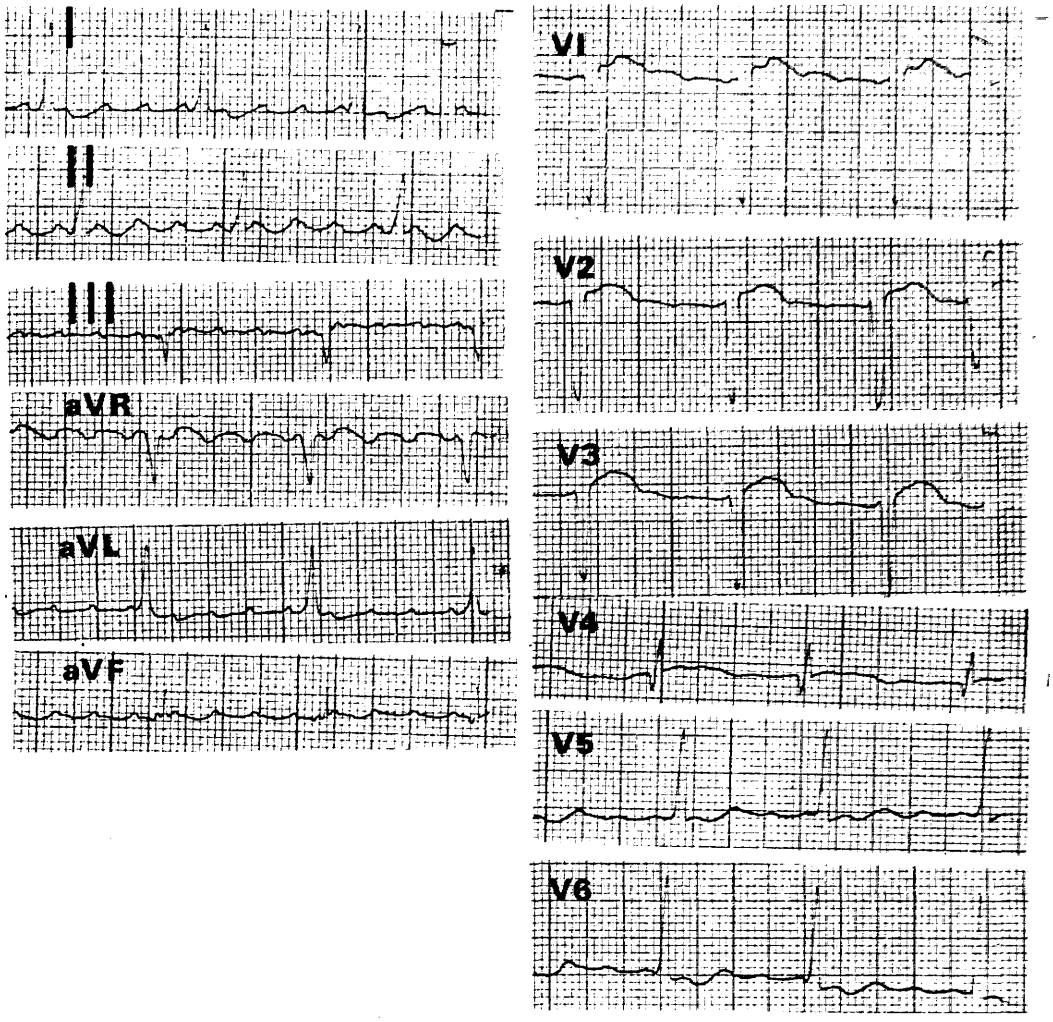


Figure 4.2

The uncommon form of atrial flutter. This 12 lead ECG shows atrial flutter with 4:1 A-V block. The sawtooth P-waves of the common form of flutter are not present, and P-waves are prominently positive in leads I, II and aVL.

4.2 Catheterisation

The patient is usually brought to the treatment room or catheter laboratory unsedated. Under local anaesthesia and sterile conditions, one or more electrode catheters are inserted transvenously. Most commonly, a median cubital (usually on the right side) or a femoral vein is used, although occasionally access has been gained via the subclavian vein. The femoral vein allows greatest ease of catheter manipulation, but is avoided in older or non-ambulant patients because of the risk of deep vein thrombosis (which has occurred in one patient in the series), and in obese patients because of the difficulties involved in cannulating the femoral vein. Most of these procedures have been carried out in the emergency pacing treatment room of the Western Infirmary, Glasgow, which contains a mobile image-intensifier for X-ray screening. This, while adequately allowing visualisation of the catheter's passage to the heart, makes it difficult to accurately assess the position of the catheter tip, because of difficulty in obtaining a lateral view. This limitation principally restricts only the accuracy of endocardial mapping of atrial flutter which could be carried out. Some patients were treated in the full catheter laboratory, with C-arm screening facilities, and more accurate maps are available in these patients (see Chapter5, section 5.6). Six different designs of multi-electrode catheter were used. These are listed in Table 4.1, and three types are illustrated in Figure 4.3.

Since intra-atrial electrogram recording is an essential part of the Atrioversion procedure, and recording and stimulation through the same electrodes is difficult due to the large electrical artifact caused by the stimulus, catheters with a minimum of four electrodes have always been used, allowing bipolar stimulation and recording. The recorded electrogram will represent activation at a site distant from the stimulation site by a distance dependent on the interelectrode spacing. For this reason, close (2mm or 5mm) spaced electrodes

TABLE 4.1

CATHETERS USED FOR ATRIOVERSION

Type	Manufacturer	Spacing	Design
TRIPOLAR			
1	Vygon	10mm	Custom built (middle electrode 10mm long)
QUADRIPOLAR			
2	USCI	10mm	Standard quadripolar
3	USCI	5mm	"Josephson" quadripolar
4	Cordis	2mm	Close spaced - custom built
5	Vygon	2/10mm	2 close spaced pairs separated by 10mm - custom built
HEXAPOLAR			
6	Elecath	10/20mm	Standard hexapolar

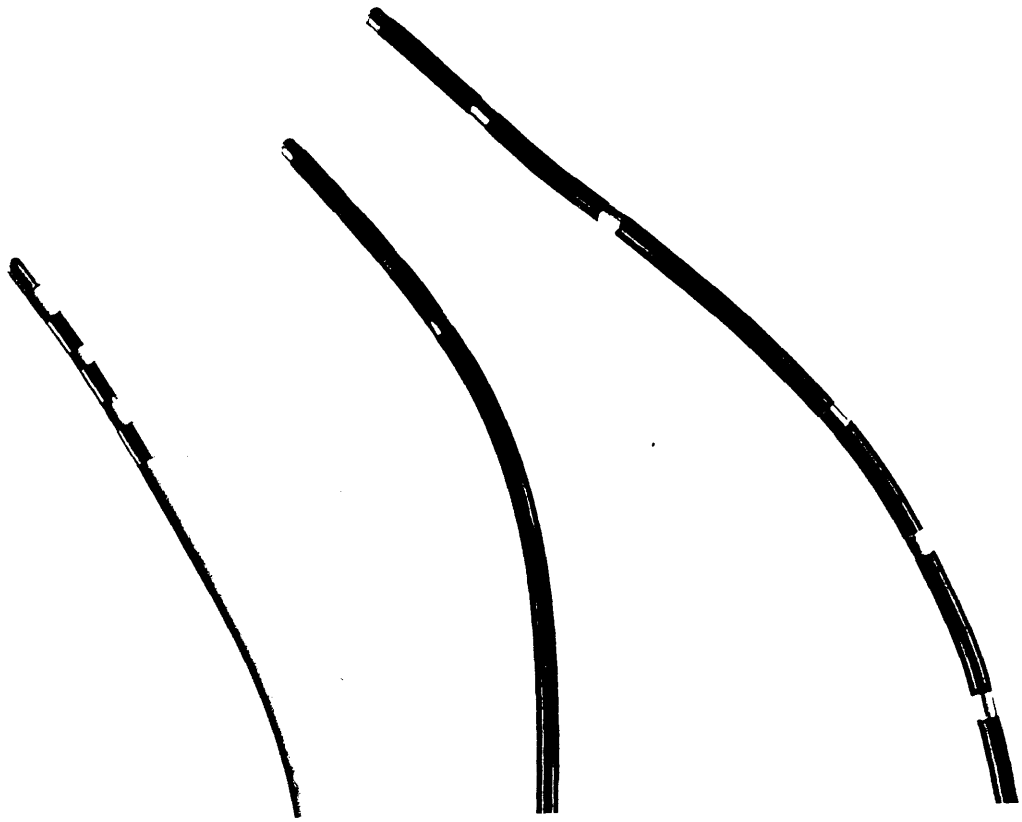


Figure 4.3

Three types of multi-electrode catheter used in this study. On the left is a Cordis quadripolar catheter with 2 mm electrode separation. In the centre is a quadripolar USCI Josephson catheter with 5 mm spacing, and on the right, an Elecath hexapolar catheter with 1 and 2 cm spacings.

were usually used, to allow activation to be recorded as close as possible to the stimulation site.

4.3 Electrophysiological investigation of the arrhythmia

4.3.1 Catheter position and mapping

The catheter is advanced to the right atrium under X-ray control, and the electrodes are connected to bio-electric amplifiers with variable gain and bandwidth, chosen to display the clearest atrial electrograms possible. Bipolar electrograms are displayed, allowing observation of local activation without interference from distant events such as ventricular depolarisation or delivery of a stimulus. However, for mapping purposes, bipolar recordings can be ambiguous, as it is often not clear whether the recording represents activation at one or other electrode, or a mixture of both (the latter being the most common case). If an endocardial map of the arrhythmia is required, then bipolar recordings should be used only if the electrodes are close spaced (5 mm or less). If a standard quadripolar catheter with 10 mm inter-electrode spacing is being used, then the exact meaning of a bipolar recording can be clarified by simultaneous unipolar recordings from each electrode. The catheter can be moved to various positions in the right atrium, and occasionally left atrial activation can be estimated by advancing the catheter into the coronary sinus. Typically, activation can be measured at up to five sites on the lateral wall of the right atrium, five on the inter-atrial septum, and five on the anterior wall (including the right atrial appendage. It is sometimes possible to estimate an endocardial activation sequence, although this may not in itself lend information to support any particular theory of the underlying mechanism of the arrhythmia, particularly in atrial flutter. This view is supported by Josephson (1979), who states that :

"Differences in atrial activation, however, have no diagnostic value in determining whether flutter is due to enhanced automaticity, micro-reentry or macro-reentry."

However, atrial mapping, when combined with electrical stimulation, can certainly help to explain the mechanisms of arrhythmias. In treating atrial flutter, the catheter is placed in a position where stable electrograms can be recorded, indicating that the electrodes are in stable contact with the atrial wall. In this study, the shorter refractory periods during atrial flutter have been found at sites where the conduction time between electrograms recorded 10 mm apart is less than 20 ms. In areas of slower conduction, electrogram amplitude is lower, and refractory periods are longer.

4.3.2 Finding the excitable window

Two electrodes are selected for delivery of the intra-atrial stimulus. An intra-atrial electrogram from a position as close as possible to the stimulation site is taken to the synchroniser unit (see Figure 4.4), which allows the stimuli to be delivered at a point in the atrial cycle determined by the delay setting chosen. The stimuli delivered are constant current, with 2 ms pulse width. Stimulation was carried out at the conventional level of 2 x diastolic threshold.

If the recording site is very close to the stimulation site, the electrogram evoked by the stimulus may be obscured by stimulus artifact on the trace. In this case it is impossible to accurately estimate its position, but capture can still be inferred by failure of the electrogram to occur at the expected time, had a stimulus not been delivered. The spontaneously occurring beats are denoted A1 (see Figure 4.5), and the depolarisation following the stimulus is called A2, with subsequent electrograms labelled A3, A4, etc. Thus the basic tachycardia cycle length can be abbreviated to A1-A1, the length of the stimulated (premature) cycle is A1-A2, and the post-stimulus cycle is A2-A3

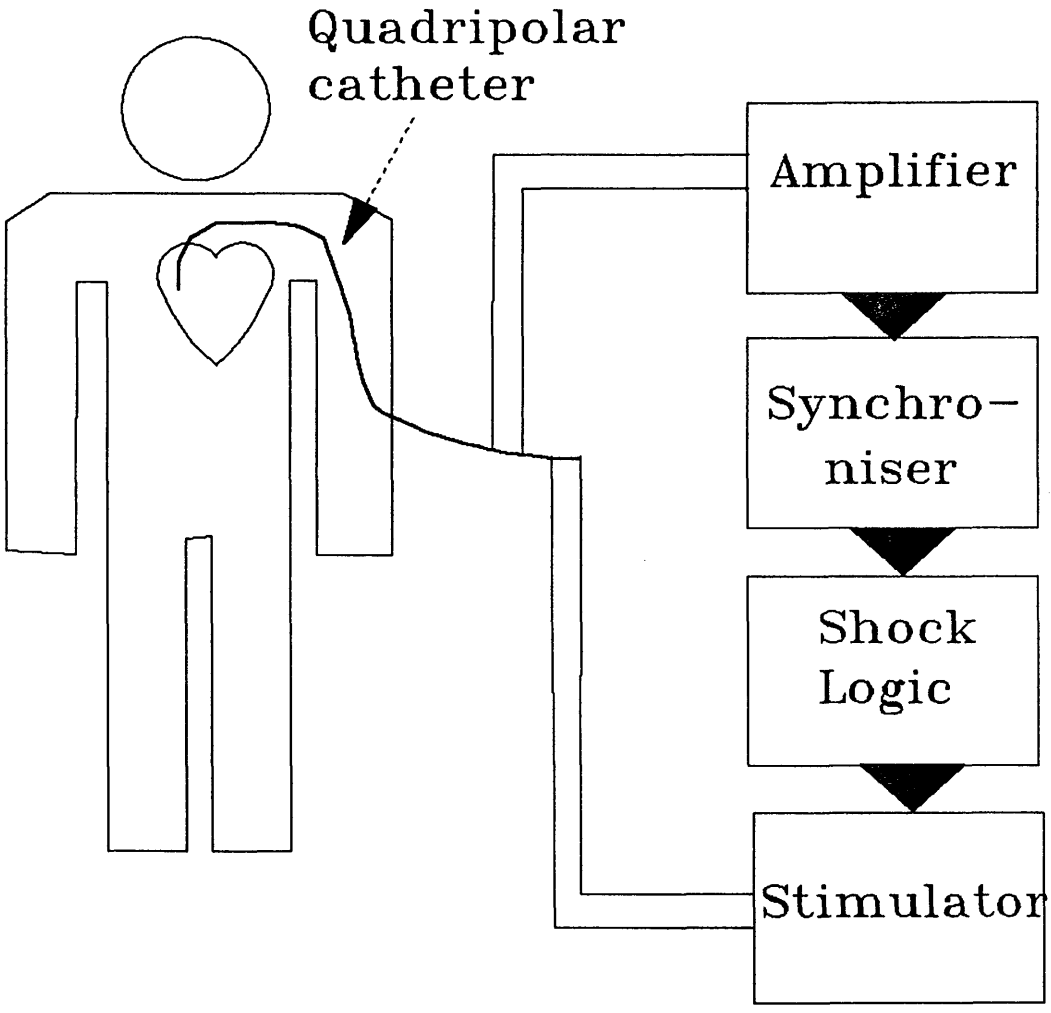


Figure 4.4

Schematic diagram of Atrioverter system.
A quadripolar catheter is placed in the right atrium. Two electrodes are connected to an amplifier, the output of which triggers a synchroniser. The stimulator output is controlled by the shock logic, which is triggered by the synchroniser output.

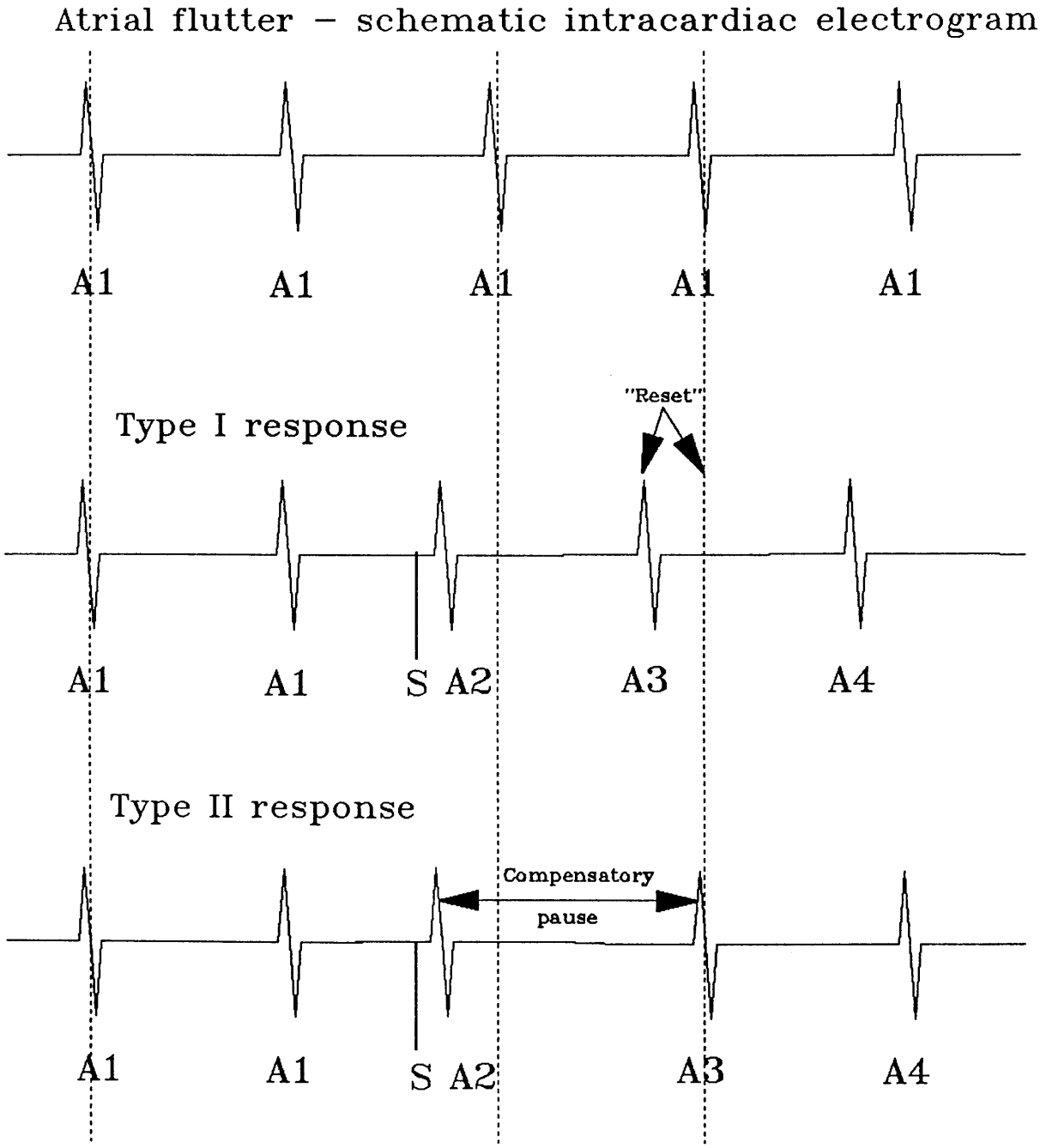


Figure 4.5

Schematic atrial electrogram during flutter.
A1 = spontaneous atrial electrograms. S = stimulus.
A2, A3, A4, etc. electrograms following stimulus.

(this cycle is often called the return cycle). The length of A1-A2 and A2-A3 are important factors in determining both the mechanism of tachycardias, and the success rate of their conversion (see Chapters 5,6 and 7). It is therefore of interest whether a stimulus has captured the atrium, and whether the tachycardia has been reset.

4.3.3 Definition of terms

The most important terms related to atrial stimulation are defined below.

> The **EFFECTIVE REFRACTORY PERIOD (ERP)** of the atrium was defined as the **longest** stimulus coupling time which failed to result in atrial depolarisation, measured at an impulse amplitude of twice diastolic threshold.

> The **FUNCTIONAL REFRACTORY PERIOD (FRP)** is defined as the **shortest** time between the previous spontaneous flutter electrogram and the evoked electrogram after a stimulus.

Examples of ERP and FRP measurement are seen in Figure 4.6

> **LATENCY** of response was said to have occurred if very premature impulses exhibited a conduction delay between stimulus and evoked electrogram which exceeded that delay seen in late diastole (see Figure 4.7).

> **CAPTURE** is said to have occurred if A1-A2 is less than A1-A1, and hence the atrial stimulation site has been prematurely depolarised.

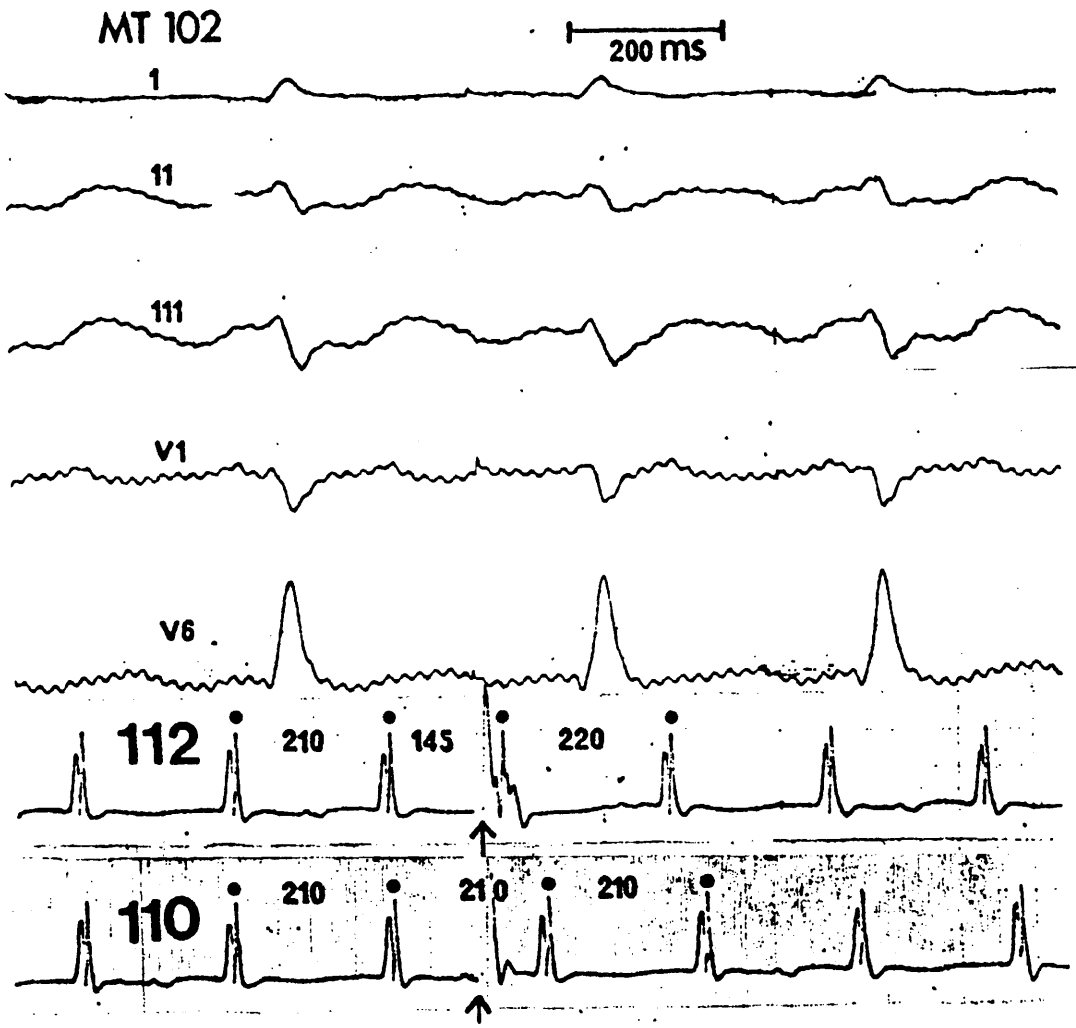


Figure 4.6

Measurements of ERP and FRP. Five surface leads show common flutter, cycle length 210 ms. The first intracardiac electrogram shows a stimulus with coupling time 112 ms, which captures, producing a response at 145 ms. This was the earliest response that could be elicited. The return cycle of 220 ms is non-compensatory (Type I response).

The lower panel shows a stimulus at 110 ms which does not capture (the timing of the next atrial electrogram is unaffected by the stimulus). Thus the effective refractory period is 110 ms and the functional refractory period is 145 ms.

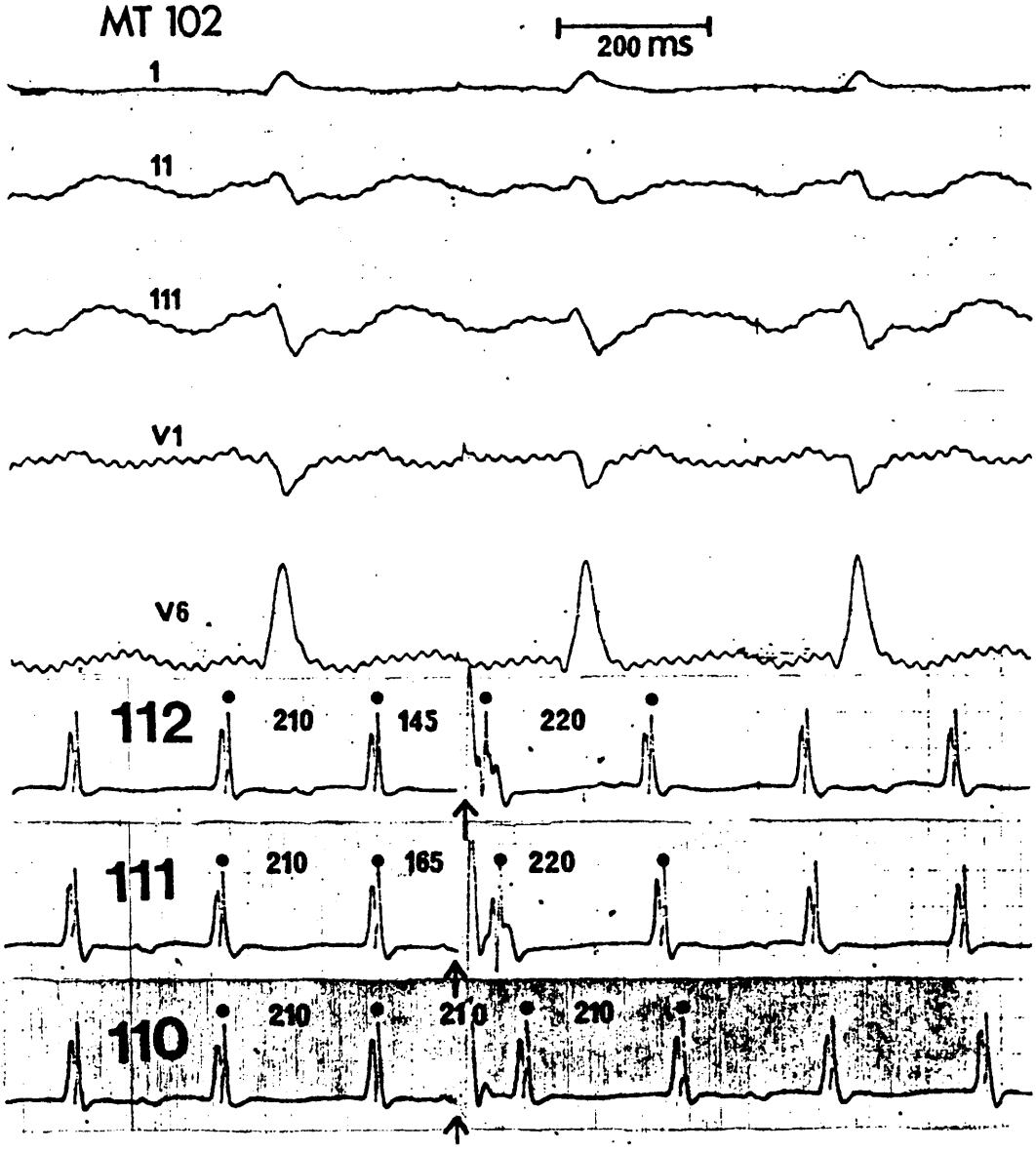


Figure 4.7

In the same patient as shown in Figure 4.6, latency of response is seen. The five surface leads show flutter with cycle length 210 ms. The top intracardiac electrogram panel shows capture during flutter with a stimulus coupling time of 112 ms. The atrium responds with an electrogram coupled at 145 ms. The lowest panel shows failure to capture with a coupling time of 110 ms. However, the central panel shows capture at 111 ms, but an atrial response at 165 ms, which is delayed by 20 ms. This illustrates both latency of response and the narrowness of the latency zone in this case.

RESET occurs if A1-A2 + A2-A3 is less than 2 x A1-A1; in this case, the return cycle does not fully compensate for the shortness of the A1-A2 cycle, and A3,A4 etc. occur earlier than would have been expected (see Figure 4.5).

When the response of the atrium to stimuli delivered throughout the atrial cycle is examined,

the period during which capture can be obtained is called the **EXCITABLE WINDOW**.

Two types of excitable window are seen.

A **TYPE I RESPONSE** or **TYPE I EXCITABLE WINDOW** occurs when the return cycle exceeds the basic cycle by less than 20 ms, and reset is apparent throughout the atrial cycle. (Figure 4.5)

A **TYPE II RESPONSE** or **TYPE II EXCITABLE WINDOW** occurs when the return cycle is longer, and only very premature beats can cause any reset of the tachycardia, or when the return cycle is always fully compensatory. (Figure 4.5)

After the initial experience indicated that a Type I site would be more likely to yield successful conversion, if an initial site exhibited a Type II response, the catheter was re-manipulated to a different site in an effort to find a Type I response. In this study, it was common to be able to find both Type I and Type II windows at different stimulation sites in the same patient. It is also possible to find Type I sites at different anatomical sites in the same patient.

The significance of the type of window found to the underlying mechanisms of atrial flutter will be discussed in Chapter 7.

4.4 Electrical conversion of the arrhythmia - Atrioversion

Having defined the excitable window, conversion of rhythm is first attempted using pairs of 2 ms pulse width stimuli, following conventional protocols. If this is unsuccessful, a third extrastimulus is added. If the patient still remains in tachycardia, as occurs in 90% of atrial flutter patients (see Chapter 5), Atrioversion is attempted. The Atrioverting shock is a constant current stimulus of long duration. The pulse width exceeds the cycle length of the tachycardia, and is chosen to be 20 ms longer than the longest return cycle seen during measurement of the excitable window. The delay is set to the earliest point during the excitable window at which capture was observed WITHOUT a conduction delay due to latency. The amplitude of the stimulus is set initially to twice diastolic threshold. If this amplitude fails to prevent re-circulation of the tachycardia impulse, which can sometimes be demonstrated by observing electrograms recorded during the long stimulus, the amplitude is increased in 1 mA increments until conversion takes place, or a maximum of ten times diastolic threshold is reached. In patients whose rhythm is not converted by Atrioversion, rapid atrial pacing following the protocol of Waldo (1977) is attempted. After conversion of rhythm, or the end of attempted conversion, the catheter is removed, and venous access sites attended. The time from beginning to end of procedure varies from 20 minutes to two hours, with a mean of one hour. Following the procedure, the patient's heart rhythm and general condition are monitored for at least 24 hours. Frequent atrial ectopics may be treated with antiarrhythmic drug prophylaxis.

4.5 Theory of intracardiac potential recording

4.5.1 Introduction

The theoretical morphology of a unipolar intracardiac electrogram has been previously described (Wilson, 1933). The electric potential recorded by an electrode a given distance from muscle in which excitation spreads linearly, is given in their equation (9).

$$V = \text{constant.} \frac{\{ (x-a)^2 + l^2 + b^2\}^{0.5} + l \,].[\{ (x+a)^2 + l^2 + b^2\}^{0.5} - l \,]}{\{ (x-a)^2 + l^2 + b^2\}^{0.5} - l \,].[\{ (x+a)^2 + l^2 + b^2\}^{0.5} + l \,]}$$

where:
V = recorded electrogram voltage
x = distance of recording point from crest of excitation wave *
2a = separation of voltage "sources" and "sinks" **
b = perpendicular distance from plane to point of recording
l = width of excitation wave width - this affects electrogram morphology little, and was assumed to be 10 cm

* This distance is measured as the projection of the total distance onto the plane of excitation, in other words, the true distance from the excitation crest is $(x^2 + b^2)^{0.5}$

** The wavefront is regarded by Wilson as being a series of voltage "sources" followed by a parallel series of voltage "sinks" at a fixed distance 2a. This distance, in effect, is related to the duration of Phase 0 of the action potential and the excitation wavefront velocity. In this study, a value of a = 1mm was arbitrarily assumed.

When radial spread of activation from a point source, such as the sinus node, is considered, then a different equation must be used. This second equation involves elliptical integrals, and is very complicated to calculate. The clinical evidence from this study does not suggest that atrial flutter is due to radial spread from a point source, and hence the simpler equation will be applied to simulate electrograms obtained in the present study.

The form of the unipolar electrogram given by the equation is shown in Figure 4.8, and is very similar to that obtained during intracardiac recordings. The

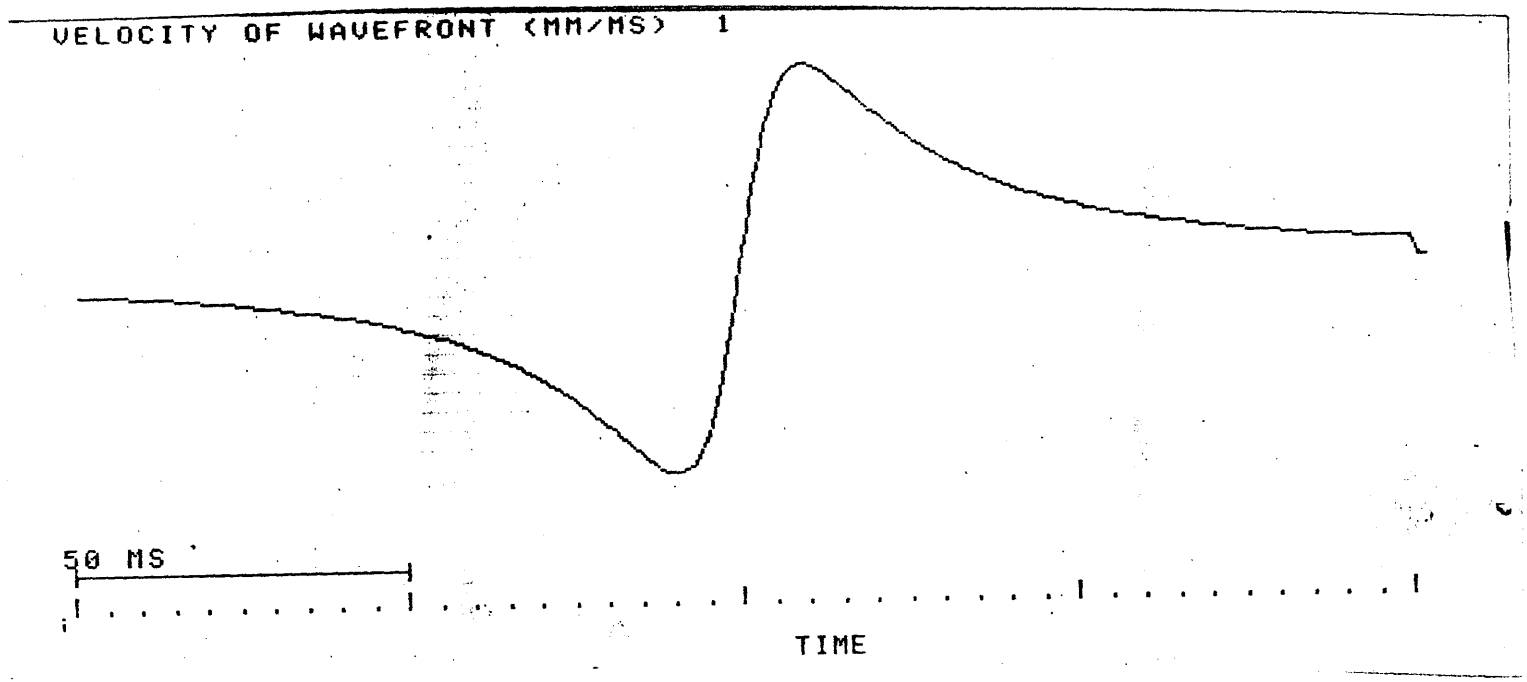


Figure 4.8

A unipolar electrogram, from the theoretical equation of Wilson, MacLeod and Barker (1933).

point at which the rapid upstroke (intrinsicoid deflection) crosses the baseline represents the time at which the tissue underlying the electrode is depolarised. Considering a second unipolar electrode close to the first, the difference between the two unipolar potentials will represent the bipolar recordings picked up by electrode catheters. If both electrodes are the same distance from the muscle tissue, the bipolar electrogram will be symmetrical, and will look like Figure 4.9. The peak of this signal indicates the time of excitation of the tissue underlying the mid point of the inter-electrode gap, as has been stated by Wellens (1980).

A computer program was developed to simulate intracardiac electrograms; relative electrode positioning and excitation wavefront velocity could be altered. The effect on the electrogram of the following parameters was investigated.

1) Variation in electrode spacing.

2) Variation in distance of the bipole from the muscle tissue.

3) Variation in the position of one electrode relative to the other.

The aim was to simulate the commonly found amplitude variation in intracardiac recordings, and to observe how much variation in the electrode position this reflected.

4.5.2 Electrode spacing

The excitation wavefront velocity was fixed at 1 m/s, in the direction of the bipole (in practice, the wavefront would move at an angle to the electrodes, but only its longitudinal resultant velocity in the direction of the bipole will produce a signal; the transverse component will cancel out). Figure 4.10 shows

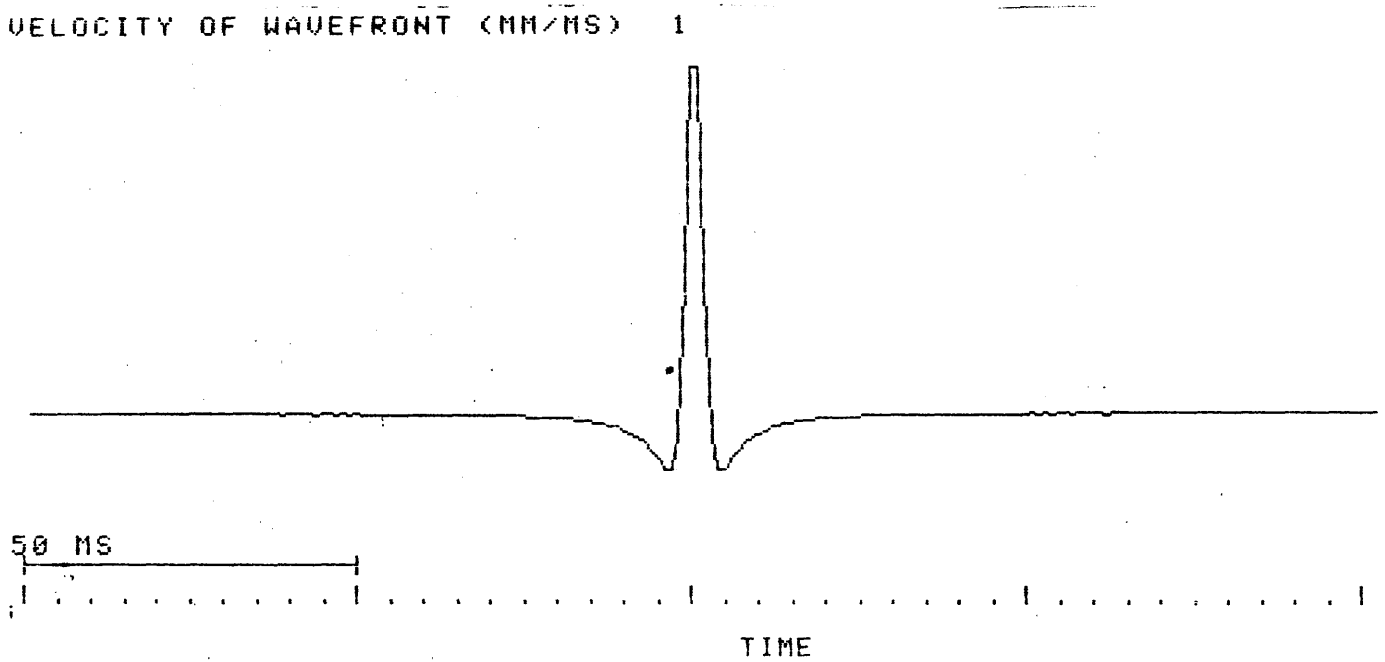


Figure 4.9

A bipolar electrogram, derived as the difference between two unipolar electrograms recorded a short distance apart.

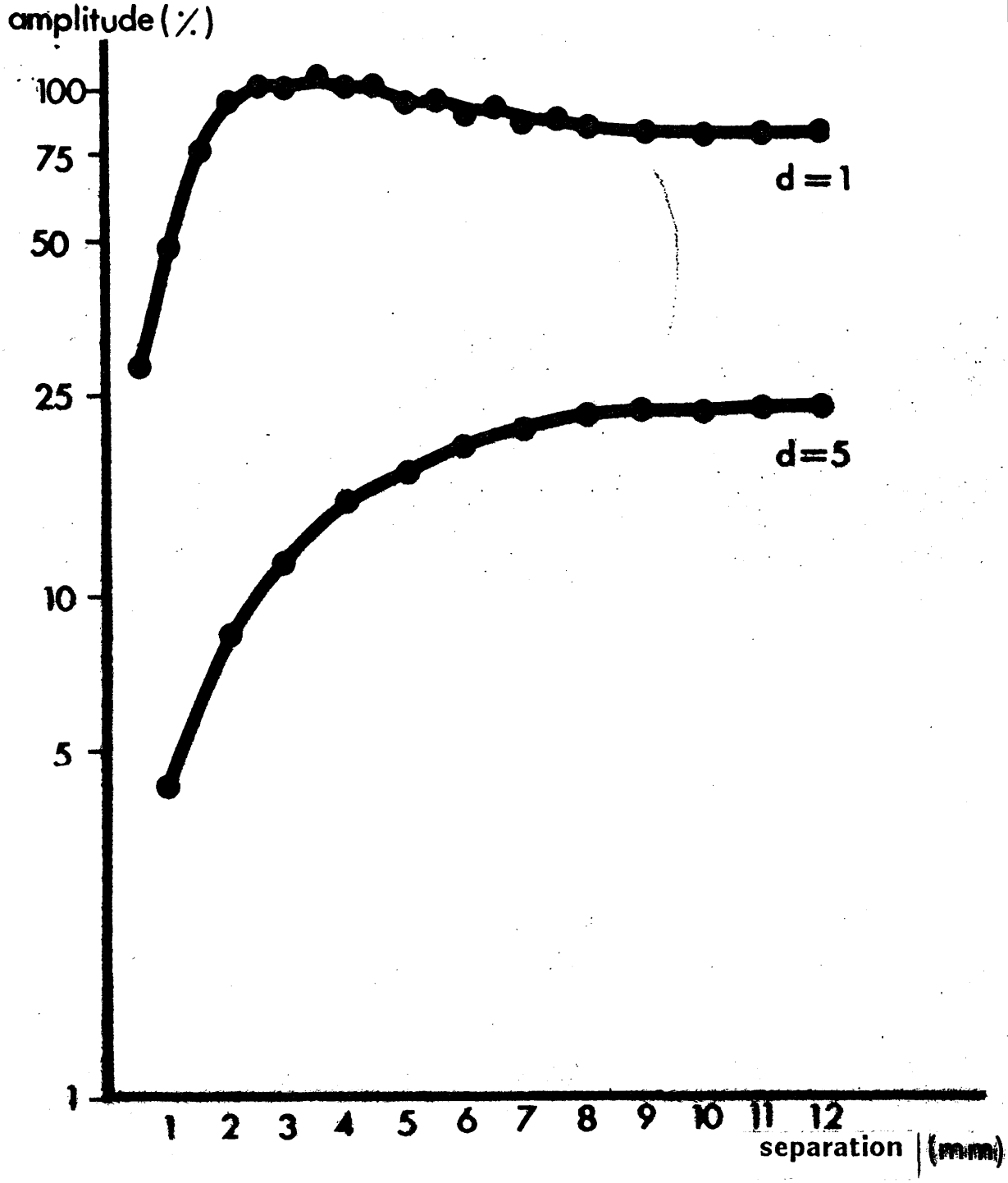


Figure 4.10

Variation in electrogram peak to peak amplitude with increasing electrode separation. The amplitude reaches a plateau at a separation related to the distance (d) of the bipole from the wall.

the effect on electrogram amplitude of varying the electrode separation (s), while keeping the distance from the muscle surface (d) constant. In the figure, s is varied from 1 to 10 mm, while d is a fixed value (upper plot 1 mm, lower plot 5 mm). The amplitude is plotted as a percentage of an arbitrary constant level, on a logarithmic scale. It can be seen that the amplitude of the signal reaches a plateau, at a separation value of 2-3 times the distance from the surface. Above this value, the peak-to-peak amplitude varies little, but of course for very large values of s, the electrogram recorded will look like two separate unipolar recordings of opposite polarity, rather than the bipolar shape of Figure 4.9. Using a wavefront velocity of 1 m/s, this does not happen until the electrode separation is of the order of 50mm. All values are proportional to the wavefront velocity, and thus a very slow wave will exhibit this splitting phenomenon even for relatively close electrode separations. This presumably results in the split potentials sometimes seen from atrial flutter sites (Cosio, 1986).

4.5.3 Distance from muscle surface

When the electrode pair is moved away from the muscle surface, the recorded amplitude will obviously fall. Figure 4.11 shows such a fall in amplitude, as the distance is increased from 1 to 6 mm. The amplitude falls to 25%. The electrode separation in this figure is 10mm. In Figure 4.12, the drop in amplitude is plotted on a logarithmic scale, for two electrode separations (1mm and 10 mm). For closer spaced electrodes, the amplitude falls off faster, and does not achieve the same amplitude as the wider spaced electrodes even at 1 mm from the surface. The fall in amplitude is not precisely exponential, but approaches this relationship for larger values of d. The rate of fall in amplitude is inversely proportional to the electrode separation.

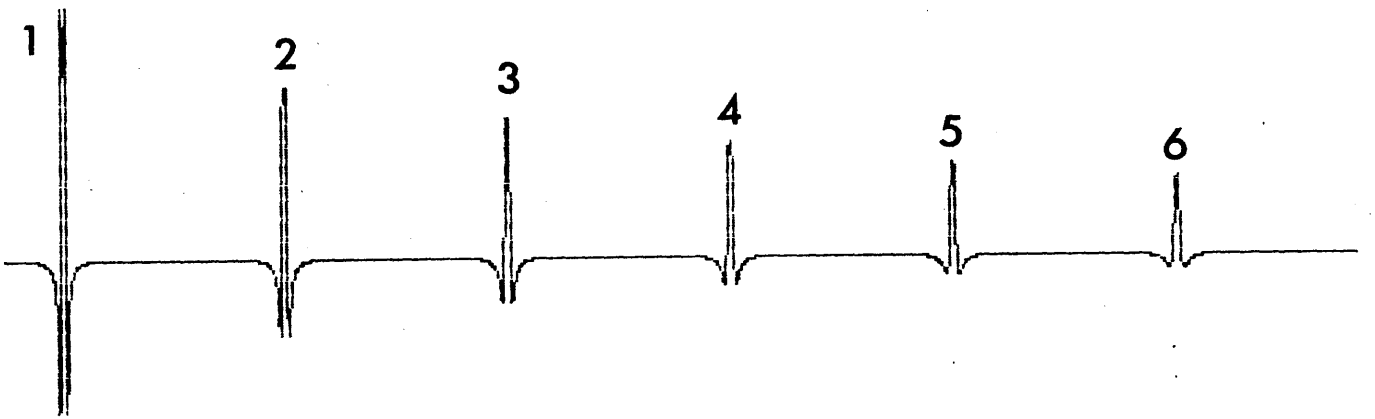


Figure 4.11

Variation in electrogram amplitude as the bipole is moved away from the wall of the heart. The electrode separation is 10 mm, and the bipole moves from 1 mm to 6 mm away from the surface. The amplitude drops to 25% of the initial value.

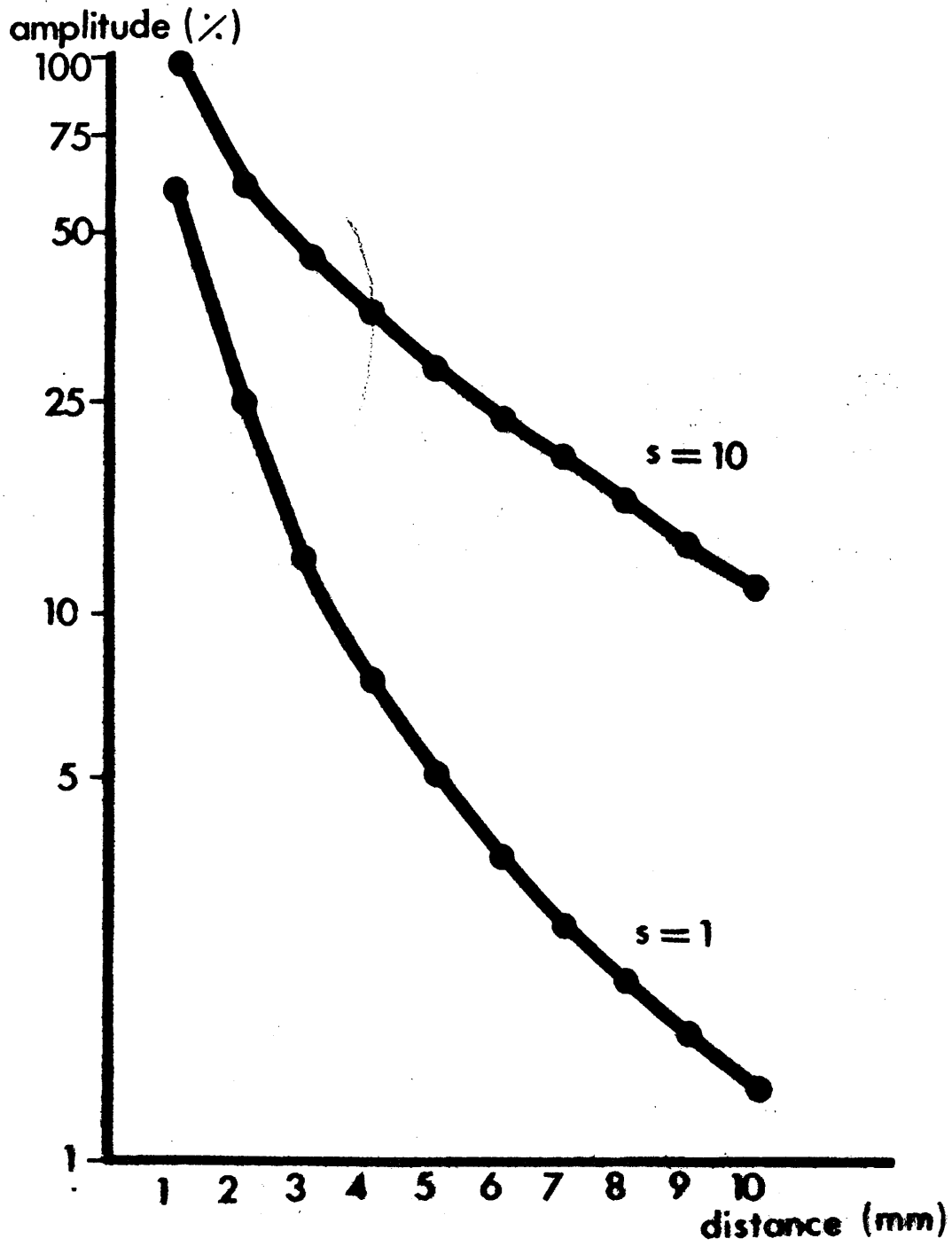


Figure 4.12

Variation in electrogram amplitude with increasing distance from the heart wall. The electrograms from close spaced electrodes (s=1 mm) decrease in amplitude faster than for wider spaced electrodes (s=10 mm). For distances over 5 mm, the fall off is approximately exponential.

4.5.4 Varying position of one electrode

In Figure 4.13, the positive electrode is 10 mm from the surface. The electrode separation is 10 mm, and the position of the negative electrode is varied from 1 to 10 mm away from the surface. As the negative electrode approaches the surface, the electrogram increases in amplitude, and looks more like a unipolar electrogram, as one would expect. The amplitude increases ten-fold with a 9 mm shift, and is exponential with respect to negative electrode distance from surface.

4.5.5 Summary

It is obvious from these results that very small alterations in electrode separation and distance from the muscle surface can make large differences in recorded electrogram amplitude. Amplitude will fall off if the electrode pair is not within a distance from the surface of approximately twice the electrode separation, and will also fall off roughly exponentially as the electrodes are moved away from the surface (faster for closer spaced electrodes). Finally, the bipolar electrogram can often resemble a unipolar tracing because the two electrodes are at different distances from the muscle surface. Cyclic variations in these factors can be caused by catheter movement (respiratory or due to ventricular depolarisation when recording in atrial flutter). Such variations need only be of small order to give a varying or alternating electrogram amplitude pattern.

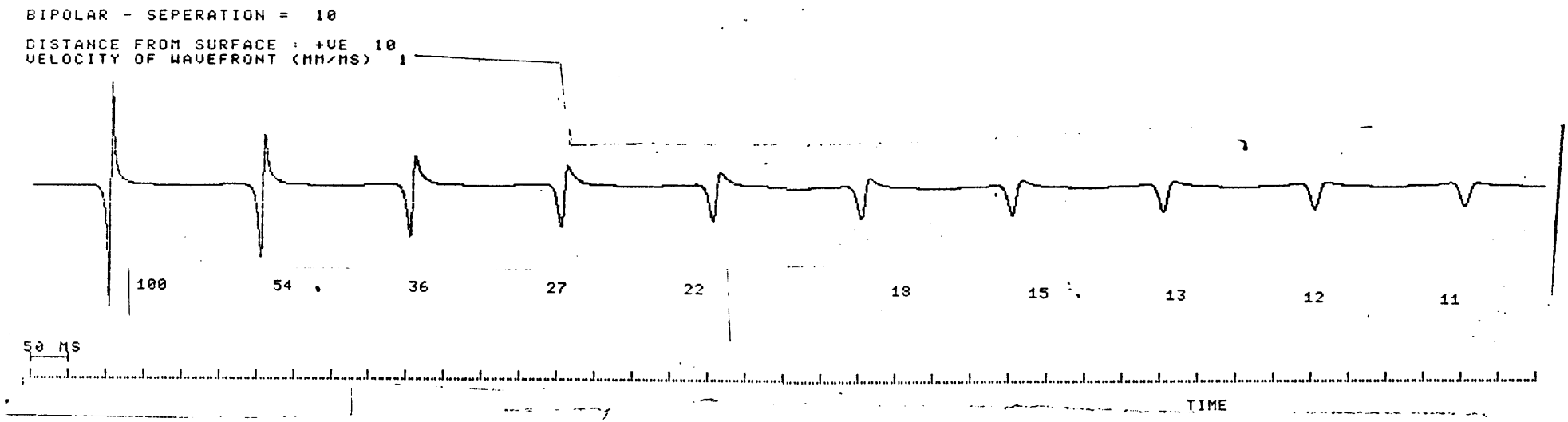


Figure 4.13

The positive recording electrode is fixed at 10 mm from the surface. The negative electrode is 10 mm away, and its position is varied from 1 mm (extreme left) to 10 mm (extreme right) from the heart wall, simulating angular variation in electrode position. As the negative electrode approaches the surface, the electrogram becomes more like a unipolar electrogram, and increases in amplitude. The amplitude is shown below the electrogram, as a percentage of the amplitude when the distance is 1 mm.

Chapter 5

MECHANISMS OF ATRIAL FLUTTER

5.1 Introduction

The mechanism of atrial flutter remains controversial, despite many efforts to verify one or other theory. As discussed in Chapter 2, it has generally been accepted that flutter is due to either discharge of an automatic focus, which, for some reason, has enhanced automaticity, or to a circulating excitation wavefront without a definable central focus. In addition, the circus movement might be very small, measuring only a few millimetres or less (micro-reentry) or it may be larger (macro-reentry). It is difficult to define the crossover point between micro- and macro-reentry from a functional standpoint, so this study will use a practical one. If it can be shown that an electrode catheter, of whatever electrode spacing, can record potentials from different points in a reentry circuit, then macro-reentry is present; if the circuit is too small to allow exploration by catheter, micro-reentry exists. The response of a micro-reentry circuit may be difficult to distinguish from that of an automatic focus, as will be shown below, and from a practical point of view, electrical stimulation could have similar results in the two mechanisms, although drug effects may be different.

5.2 Response to stimulation

5.2.1 Macro-reentry circuit

In the classical model of a reentry circuit (Figure 5.1), the head of the circuit is a depolarisation wave, and the tail is the repolarising tissue. In the "leading circle" version of reentry (Allessie, 1977), the wavefront takes the shortest possible path through the tissue. Thus the radius of the circuit is determined by the refractory properties of the tissue, because the circulation time, and hence path length, must be long enough to allow recovery of all the tissue in it.

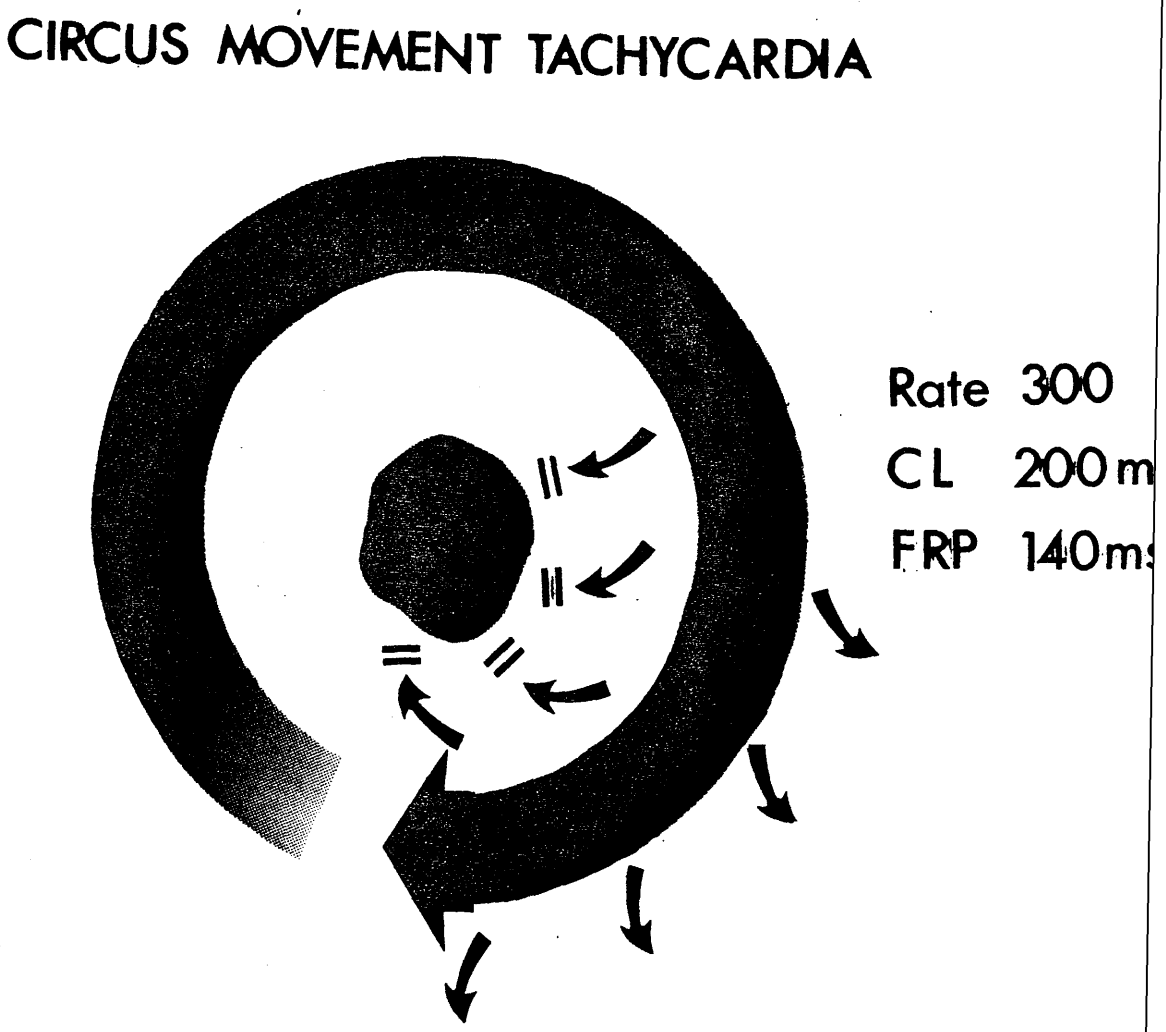


Figure 5.1

A circus movement tachycardia. The depolarisation wavefront (arrowhead) chases the receding "tail" of refractoriness. There is a central area of block around which the impulse circulates. In this, and the following figures, the cycle length (CL) of 200 ms and functional refractory period (FRP) of 140 ms are assumed to simplify the discussion.

Allessie (1977) suggested that this means that there is no "excitable gap" between the head and tail of the circuit; however, he also showed that non-uniform refractory periods must exist in order for a circus movement to be initiated. It follows, then, that there will be no excitable gap at the point in the circuit with the longest refractory period. Other points in the circuit will have an excitable gap whose duration is a measure of the disparity in refractoriness. Of equal importance, at some points of the circuit, the tail will only just have recovered its excitability when it is depolarised again by the head. Here, the depolarisation will occur in the relative refractory period. At the cellular level, this will produce action potentials of decreased amplitude, and it may well be the case that the wavefront will have a lower stimulating efficacy when the refractory period is long. If a stimulus of greater potency, for instance a high current electrical pulse, is applied, then stimulation earlier in the cycle may be possible, although the circuit head would not be able to propagate at such a short coupling time. For both these reasons, it is likely that an excitable gap will exist in atrial flutter even if it is due to a macro-reentry circuit of the so called "leading circle" variety.

In Figure 5.2, a macro-reentry circuit with cycle length 200 ms is seen. For simplicity, the flutter cycle length will be taken as 200 ms in all further discussion. The arguments raised apply, however, to all cycle lengths. There is an excitable gap between head and tail, and during that gap, a stimulus is applied (at the site marked *). The stimulus will capture the tissue, and will propagate forward (orthodromically) through the excitable tissue. There will be backward (antidromic) conduction also, but collision will occur with the head of the circuit. In effect, this terminates the arrhythmia, but the orthodromic impulse simultaneously restarts it. The orthodromic impulse is early, and will, at some point, encounter the tissues with the longest refractory period. If the impulse has an enhanced stimulating potency, or these tissues have an excitable gap, then they will respond. The return cycle following the premature beat will

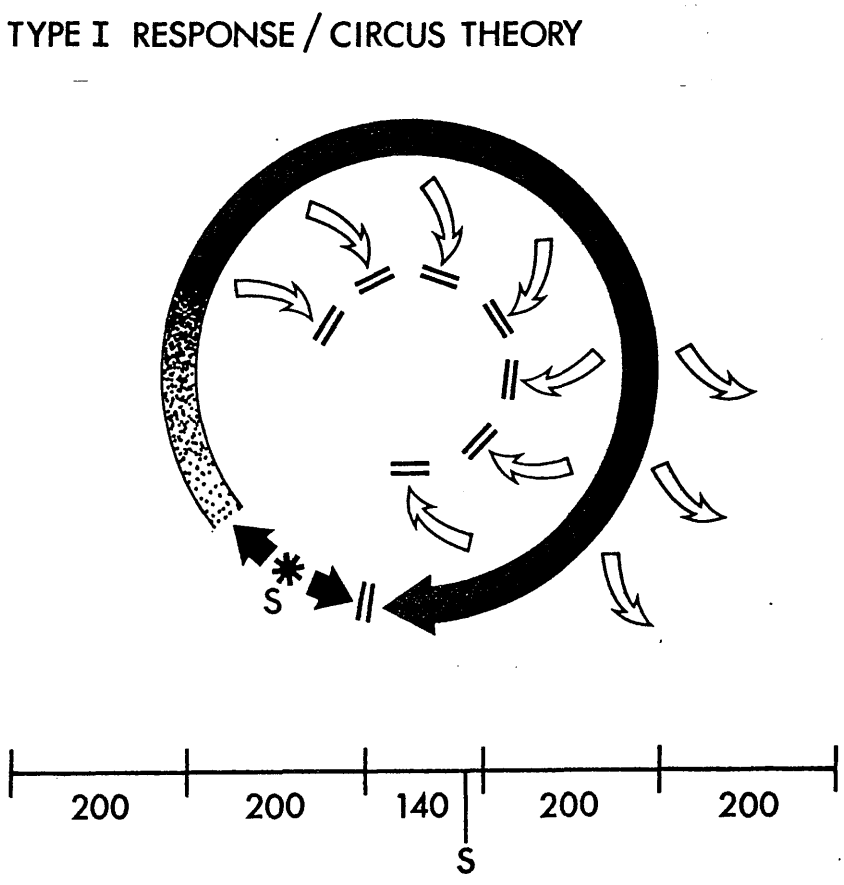


Figure 5.2

A Type I response in a circus movement tachycardia. A stimulus is delivered to a site within the circuit (marked '*'), and induces a premature beat, which propagates antegradely without delay, giving a 200 ms return cycle. There is retrograde block with the spontaneous circulating wavefront.

have the same length as the basic cycle - a non-compensatory pause. This corresponds to the "Type I" response defined in Chapter 4 (Section 4.3.2). If, however, the sites with the longest refractory periods are distant from the stimulation site, the impulse, having been conducted prematurely through a substantial part of the circuit, will have the same or less potency than the normal circuit head. Accordingly, one of two things will happen.

1) The circus movement will terminate. If no excitable tissue is available, the wavefront will be extinguished. This is illustrated in Figure 5.3.

2) The wavefront will take a longer path during this premature cycle, in order to find excitable tissue. In effect, it will skirt around the inexcitable area (Figure 5.3). This may lead to a degree of lengthening of the return cycle; how much lengthening occurs depends on the length of the "detour", and the relative conduction speed in the detour pathway.

In Figure 5.4, a stimulus is applied to a site which is some distance away from the circuit. The distance is defined by the conduction time from the site to the nearest excitable point of the circuit. If this conduction time is t, then an atrial premature beat will take time t to reach the excitable gap in the circuit, and after a cycle of 200 ms, will again take time t to return from the circuit to the site - for simplicity, assume that the conduction times in both directions are the same, although this may not be strictly accurate. This assumption is made when measuring sino-atrial conduction time by the extrastimulus method. It follows that the return cycle will measure (200 + 2t), in the absence of any conduction delay of the premature beat. Accordingly, if the return cycle is measured, and t is calculated, then this value will represent the maximum

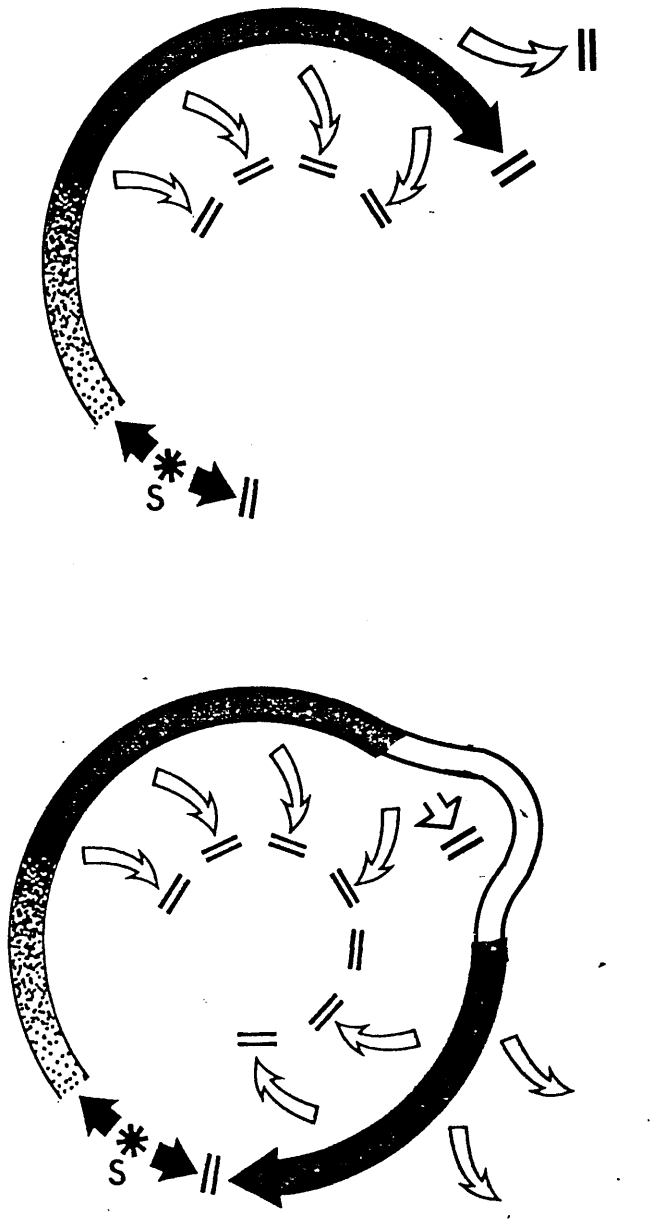


Figure 5.3

Responses of a circus movement tachycardia to a premature beat when part of the circuit has a long refractory period. The premature beat cannot be conducted through this area (upper right of circuit), and will either be blocked, thus terminating tachycardia (upper panel), or will "detour" around the inexcitable area to find non-refractory tissue, thus prolonging the return cycle (lower panel).

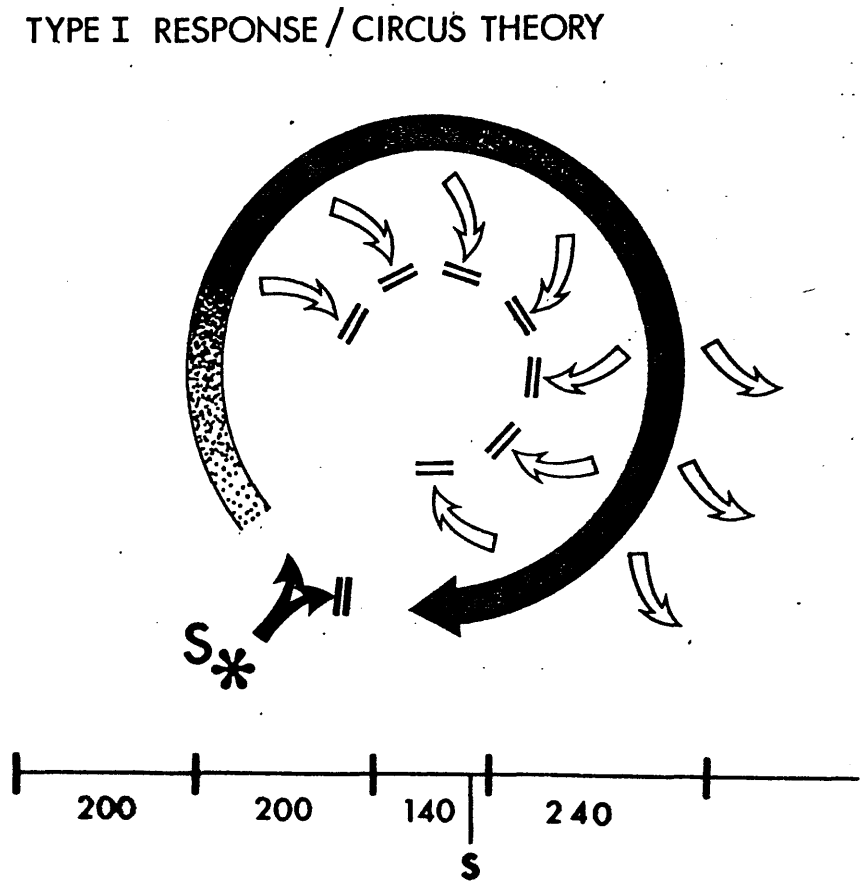


Figure 5.4

Stimulation at a point close to, but not within, a reentry circuit. The premature stimulus (S) is able to penetrate the circuit, as in Figure 5.2, and is propagated without delay, but the return cycle will be prolonged by twice the conduction time (t) from the stimulation site to the circuit. In this case, t = 20 ms, and the return cycle = 240 ms.

possible conduction time from the atrial site to the circuit. Any occult delay in conduction will increase the measured t value, but the true value will never exceed the measured value, since the premature beat cannot take a "short-cut" around the circuit. It is possible to have a large value of t, if a site is distant from the circuit. In such a case, it may not be possible for a premature beat to invade the circuit, and collision of the premature and circulating impulses will occur at an intermediate point (Figure 5.5). If the refractory period at the stimulation site is R, then a fully compensatory response will always occur if:

$$2t > (200 - R)$$

Thus a long refractory period, or a distant site with large t, will always show fully compensatory pauses when an extrastimulus is applied. Even if $2t < 200 - R$, a fully compensatory pause may still occur in response to ectopics late in the atrial cycle, or if there is tissue between the site and the circuit which has a long refractory period. Note that the return cycle measures at least $(200 + 2t)$, and theoretically a very premature impulse could encounter conduction delay leading to a greater than compensatory pause. Such a phenomenon would be the only possible evidence to prove that conduction delay exists.

In summary, the response of a macro-reentry atrial flutter circuit to a premature atrial beat depends on the prematurity of that beat, and the positioning of the atrial site relative to the circuit. Four responses are possible:

1) termination,

2) return cycle equal to basic cycle,

3) return cycle prolonged,

4) return cycle fully compensatory.

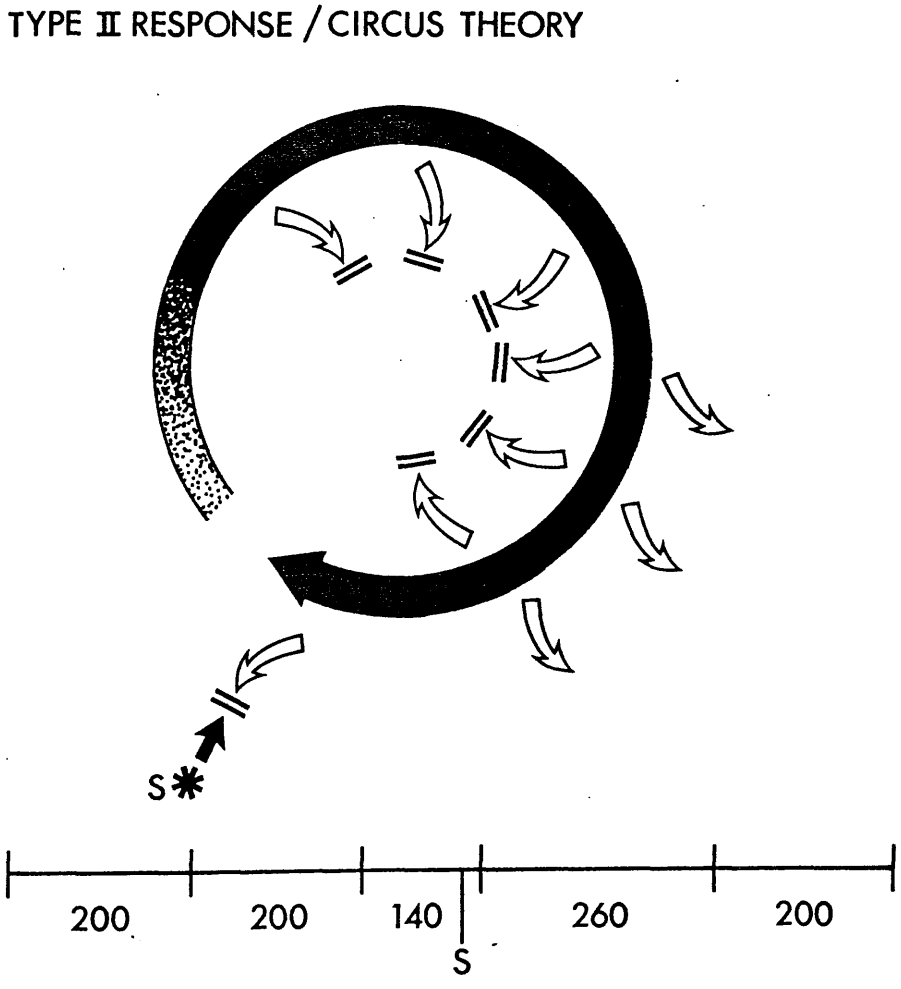


Figure 5.5

Stimulation remote from the reentry circuit. The conduction time to the circuit (40 ms) and the refractory period of 140 ms do not allow a premature beat (S) to penetrate the circuit. Collision occurs in intervening tissue, and a fully compensatory pause is seen.

There are also three types of atrial site:

1) distant from the circuit ($2t > 200 - R$)

2) close to the circuit ($2t < 200 - R$)

3) in the circuit ($t = 0$).

The possible results of extrastimulation are shown in Table 5.1, and an asterisk against a response implies that such response would depend on the occurrence of conduction delay. It can be seen that the only "diagnostic" response is a return cycle equal to the basic flutter cycle length - this can only occur if the stimulation site is within the reentry circuit. Not surprisingly, termination is suggestive that the site is in, or close to, the circuit, and a fully compensatory pause is more likely to occur with later ectopics or at more distant sites. It will be recalled from Chapter 4 that a Type I excitable gap was defined to be present if the return cycle did not exceed the basic cycle by more than 20 ms. In the absence of conduction delay, this implies that a Type I site has a conduction time to the circuit of no more than 10 ms. A Type II site has longer return cycles, and although these could occur with conduction delay at sites close to the circuit, a Type II site is likely to be a more distant site. Thus Type I sites will always be close to the circuit, while Type II will normally be far from the circuit, but, on occasion, will be close sites exhibiting conduction delay.

5.2.2 Micro-reentry circuit

Since a micro-reentry circuit is too small to allow exploration with an electrode catheter, it will not be possible to stimulate at a site within the circuit, and the conduction time t will always be greater than zero. If t is small, however, the return cycle will not be compensatory, and, as with a macro-reentry circuit, a Type I response may be seen if $t < 10$ ms. Fully

Table 5.1

MACRO-REENTRY CIRCUIT

Possible responses to extrastimulation

POSITION OF ATRIAL STIMULATION SITE

	In circuit	Close to circuit	Distant from circuit
TYPE OF RESPONSE	t = 0	2t < 200-R	2t > 200-R
Termination	Yes	Early	x
Return cycle = basic cycle	Yes	x	x
Return cycle longer than basic cycle (not fully comp.)	Early*	Early	x
Return cycle fully compensatory	Late*	Early*/Late	Yes

Key:

*	- response only occurs if occult conduction delay exists
200	- flutter cycle length (ms)
R	- refractory period of stimulation site
x	- response not possible
early	- ectopic beats induced early in the atrial cycle
late	- ectopics induced late in the cycle

compensatory responses will be seen at distant sites. Since the circuit is very small, it will be difficult to position a catheter close to it, and thus difficult to achieve a Type I response. Most atrial sites will be likely to show a Type II response. The probability of finding a Type I response when applying stimuli near to any reentry circuit is likely to be proportional to the mass of tissue involved in the circuit.

5.2.3 Automatic focus

An automatic focus is a cell or group of cells which continuously discharges. In natural pacemaking cells such as those of the sino-atrial node, this is due to self-depolarisation during Phase 4 of the action potential (diastole). If an automatic focus is present in atrial flutter, the rapid rate of depolarisation implies that the diastolic phase is short, so the rate of self depolarisation must be high. On the other hand, the mechanism of self-depolarisation may differ in a very rapid automatic focus; one possibility is that neighbouring cells are "out of phase", such that while one has just recovered excitability, a neighbouring cell is depolarising - this phenomenon has been termed "reflection", and if present at a cellular level, might be able to sustain an ectopic rhythm. However, the mechanism of the enhanced automaticity present in an automatic focus probably does not affect its response to electrical stimulation. It is clear that, as above for micro-reentry, an extrastimulus applied to a site distant from the focus will be followed by a fully compensatory pause, because there will be collision between the wavefronts originating from the focus and the stimulus (Figure 5.6). However, at sites close to the focus, it may be possible for an ectopic beat to propagate to the focus before it depolarises, and stimulate it during its relative refractory period (Hoffmann, 1960). If this premature stimulation of the focus is above threshold level, it may cause one of three responses:

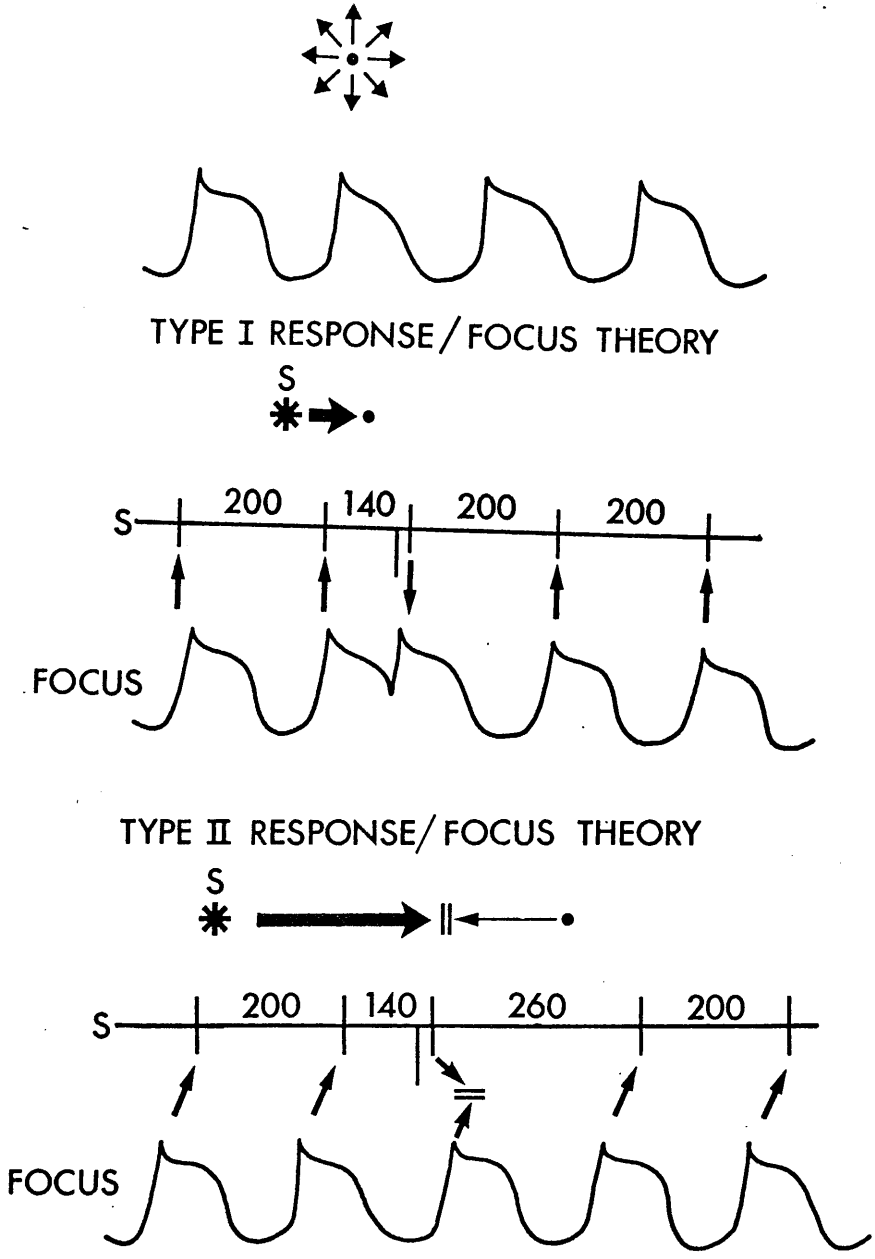


Figure 5.6

An ectopic focus discharging 300 times per minute. The focus, and a schematic of its transmembrane action potential are shown in the upper panel. In the centre panel, a stimulus (S) very close to the focus prematurely discharges it, and the return cycle is not prolonged (Type I response). In the lower panel, the stimulus site is remote, and the intervening tissue "protects" the focus from premature discharge. Collision of impulses occurs, and a fully compensatory pause results.

1) The focus may cease its activity and the tachycardia will terminate; if the focus possesses true pacemaker activity, this is an unlikely response.

2) The premature action potential will have the same duration as the normal action potential of the focus. In this case, the return cycle at the stimulation site will exceed the basic cycle by twice the conduction time t, as for a macro-reentry circuit (see Figure 5.6).

3) Due to its prematurity, the evoked action potential is likely to be of lower than normal amplitude, and may be of shorter duration (Hoffmann, 1960). The former condition will lead to delayed propagation and probable prolongation of the return cycle, but the latter condition would tend to shorten the return cycle. Thus the precise effect on the return cycle will be difficult to predict, but prolongation is most likely, and to full compensation may occur.

If the second of these responses occurs, and the conduction time t is less than 10 ms, then a Type I response will be seen. However, if these conditions are not met, a Type II response is likely occur.

5.2.4 Determining the mechanism of flutter by extrastimulation

Since Type I and Type II responses can be found with both reentry circuits and automatic foci, it would at first appear that such responses cannot differentiate between the mechanisms. However, recalling the definition of macro-reentry, if potentials can be recorded from different parts of a circuit, it may be possible also to stimulate different parts of the circuit. This would

be manifest by finding Type I responses at more than one atrial site, differing in location, and, more importantly, differing in activation time. Such a finding would not be compatible with micro-reentry or an automatic focus, since all activity in these models originates in one small area, with radial spread of activation; it will not be possible to affect a focus other than during its relative refractory period, which will be at a specific fixed point in the flutter cycle, and will not vary with anatomic location of the stimulation site.

5.3 Form of atrial flutter : "common" vs "uncommon"

5.3.1 P-wave axis in atrial flutter

The principal difference between the two clinically observed forms of atrial flutter is in the P-wave axis on the surface electrocardiogram. In the common form of flutter, the main atrial deflections are large, negative, sawtooth waves in leads II and III, suggesting that the course of activation is mainly towards the patient's head. The P-wave has variable form in the chest leads, and is usually easiest to see in the anterior leads (V1 and V2), where it is commonly positive or biphasic. This would suggest that the activation proceeds anteriorly for at least part of the cycle, and has led to the contention that the common form of flutter may be due to an automatic focus situated low and posteriorly, probably in the left atrium (Mirowski, 1967) or coronary sinus (Rosen, 1969). In contrast, the uncommon form has a very different atrial activation axis, with positive P-waves in the limb leads, and again variable P-waves in the chest leads. Again, vectorially, a high atrial automatic focus site would be suggested. Also, the P-waves in the uncommon form are more discrete than the continuous, undulating atrial waves in the common form; this has led to the suggestion that, even if reentry underlies the common form, enhanced automaticity is responsible for the uncommon form. However, Boineau (1976) showed that surface activity did not always accurately reflect intracardiac events. If there is a radial spread of activation in all directions at a particular

time, the net vector will be zero, and no activity will be apparent on the surface ECG. This "pseudo-asystole" does not reflect atrial quiescence, and only intracardiac mapping can give a true picture.

There have been no reports in the literature of both forms of flutter existing in the same patient. Such a finding would either imply that the patient's atria can have more than one automatic focus in different areas, producing different P-wave axes, or that two different circuits are present, whose different pathways account for the surface activation change. It is also possible that a combination of an automatic focus and a reentry circuit might be present, but this seems less likely.

5.3.2 Atrioversion series - conversion of P-wave morphology

In 7 of the cases in the present series, the common form of flutter has been converted to the uncommon form using electrical stimulation. In cases 17, 31, 69, 73 and 77 this was achieved using a single extrastimulus. In case 41, three extrastimuli were applied, and in case 27, a long Atrioverting impulse was given. In one case (case 25), the uncommon form was converted to the common form by a single extrastimulus.

Case 17

Figure 5.7 shows an electrogram from the mid lateral right atrium and surface lead III. Atrial flutter is present with a cycle length of 270 ms. A single premature beat in the mid right atrium, coupled at 150 ms, is followed by a non-compensatory pause, and conversion of flutter type. The surface P-wave is now bi- or polyphasic in lead III, and the atrial electrogram has the opposite morphology (it is now biphasic positive-negative, instead of negative-positive). Unfortunately, only lead III has been recorded, because the FM tape recording of leads I and II was faulty. Lead II showed a more typical broad negative flutter wave initially, and was small and positive after conversion. In Figure

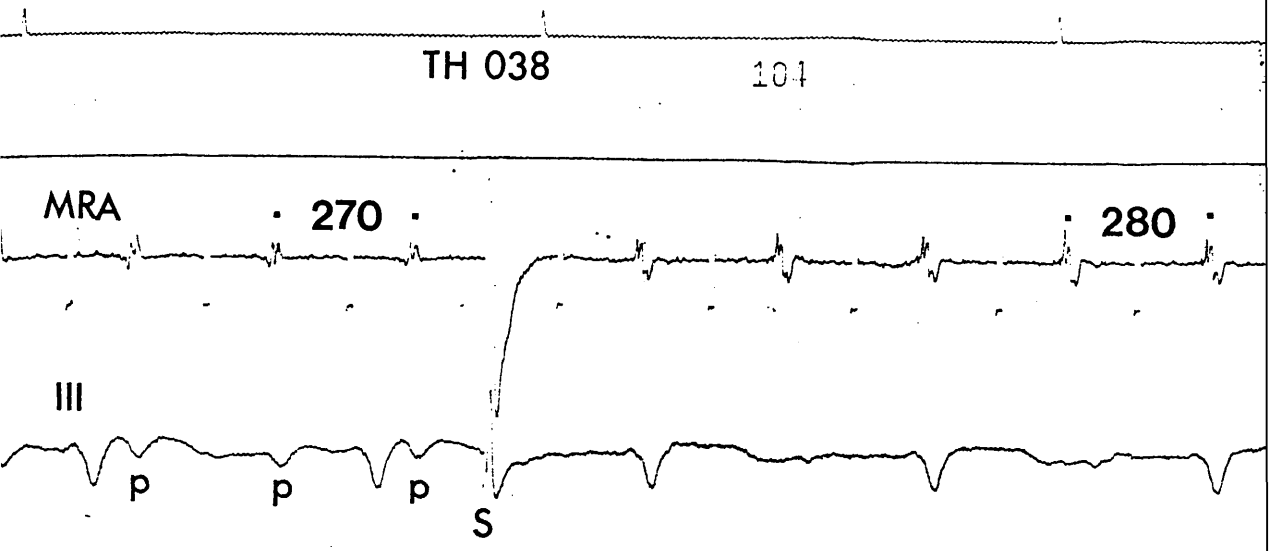


Figure 5.7

Case 17. Surface lead II and a mid right atrial electrogram during slow atrial flutter (cycle length 280 ms). Following an atrial stimulus (S), there is reset of the flutter cycle and alteration of P wave morphology in both surface and intracardiac leads.

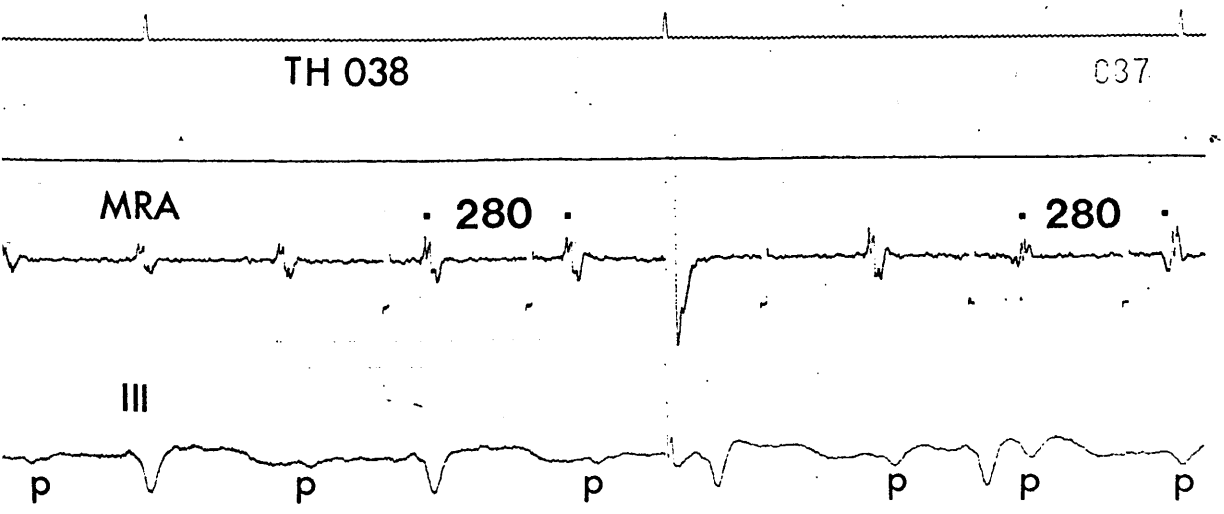


Figure 5.8

Case 17 (see Figure 5.7). A further atrial stimulus returns the flutter pattern to its original morphology on both surface and intra-atrial recordings.

5.8, a further stimulus is applied to the same patient, and the flutter P-wave axis reverts to the initial pattern. It is interesting in this trace that the stimulus, coupled at 185 ms, is followed by an apparently fully compensatory pause, and the next intracardiac electrogram from the mid right atrium has unchanged morphology - it is positive-negative. However, the surface P-wave has already reverted back to the negative waves seen in the first half of Figure 5.7. In subsequent cycles, the intra-atrial electrogram also changes its morphology, returning to negative-positive. The exact mechanism of this conversion of flutter type obviously cannot be explained from one intracardiac trace, but it is nevertheless clear that two atrial tachycardias with closely similar rates can be interchanged by delivering a single extrastimulus.

Case 41

In Figure 5.9, a fuller set of traces may help to explain this phenomenon. This patient had the common form of flutter, with negative P-waves in II and III (indicated by solid arrows), and a cycle length of 205 ms. Three atrial electrograms are shown, from the mid and low right atrial lateral wall (MRA and LRA), and from the low inter-atrial septum (LAS). The LAS trace also shows prominent ventricular deflections. Atrial activation of LAS precedes activation in MRA and LRA by 40 ms (sloping arrows). Three stimuli are given to the mid right atrium. These all successfully capture, as can be seen in the LAS trace; there is an increasing degree of conduction delay (latency) between the stimulus and the evoked LAS response. After the stimuli, the following observations can be made:

1) The flutter cycle length (205 ms) is unchanged.

2) The P-wave axis on the surface leads has altered - there are now positive P-waves in leads I and II (open arrows).

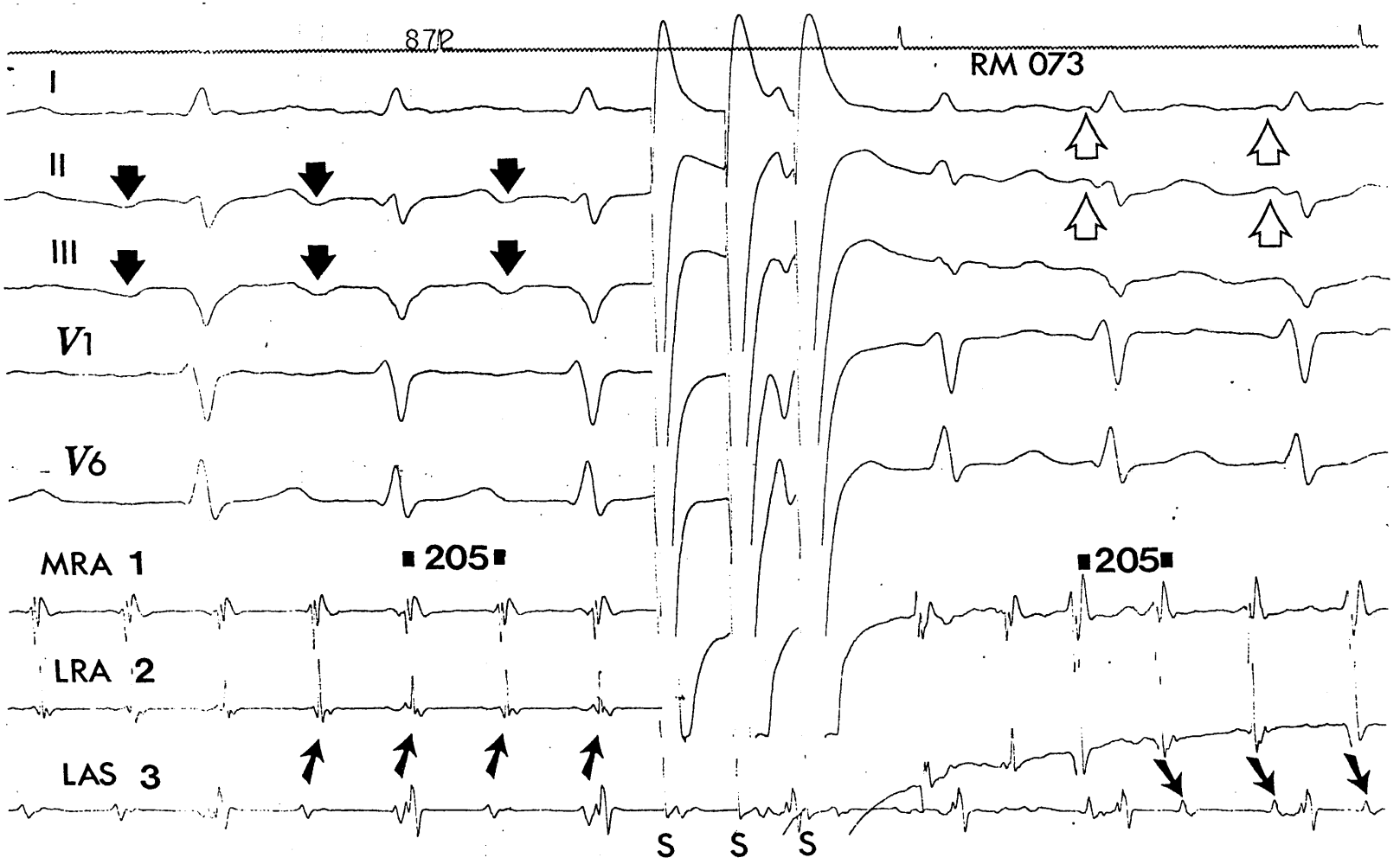


Figure 5.9

Five surface and three atrial electrograms show common atrial flutter (Case 41). Three extrastimuli to the mid lateral right atrium convert the P wave in the surface leads to the uncommon form of flutter. See text for discussion.

3) The morphology of the atrial electrograms show slight but minimal alterations.

4) The LAS trace now shows activation 40 ms after MRA and LRA - confirmation of the change in activation pattern inferred from the surface ECG.

5) There is a brief (300 ms) spell of disorganised atrial activity in the low septal trace immediately after the stimuli, and before re-organisation into the new form of flutter.

In this case, it was not possible to convert the uncommon form of flutter back to the original form. This trace confirms that it is possible to convert flutter from the common to uncommon form with electrical stimulation, without changing the rate. The mechanism may be an induced conduction delay, or block, in a macro-reentry circuit; in this case, the block may be occurring between lateral wall and low septum. In some cases, such a block would probably cause termination of flutter, but in these cases, a new circuit may have become established. It is difficult to reconcile these results with the presence of an automatic focus. If this were the case, then one would have to postulate that it was possible for electrical stimulation to extinguish a focus low in the atrium (common form of flutter) and simultaneously initiate another focus high in the atrium (uncommon form), with the same rate of discharge; such a result seems very unlikely. Alternatively, the conduction pattern from a single focus may be altered by stimulation such that the activation pattern spreading from the focus gives rise to a different surface P-wave morphology. This phenomenon is a theoretical possibility, and is common in ventricular tachycardia, but is undocumented in supraventricular

arrhythmias. In the remaining 6 cases, the pattern was similar to case 41 - one form of flutter was irreversibly converted to the other.

Further electrical stimulation led to conversion to sinus rhythm in 3 cases (1 using extrastimuli, 2 using Atrioversion) and to sustained atrial fibrillation in 4 (1 by extrastimuli, 3 by Atrioversion).

It is commonly held that arrhythmias due to enhanced automaticity are not reliably induced or terminated by using programmed stimulation (Josephson, 1979). Bearing this in mind, these eight conversions of one form of atrial flutter to another lend some support to the contention that flutter is not due to enhanced automaticity.

5.4 Atrial stimulation during flutter

5.4.1 Introduction

As described in Section 4.3.2, the effective refractory period (ERP) is the longest coupling time of a stimulus (S) which fails to result in an atrial premature beat. In addition, the functional refractory period (FRP) was measured; this is defined as the shortest coupling time between a flutter beat (A1) and an induced atrial ectopic beat (A2). This is always longer than the ERP, and is a measure of the most premature physiological impulse which can be induced at a stimulation site. Because of latency with very premature stimuli, the shortest A1-A2 often does not concur with the shortest A1-S.

The refractory periods were analysed using a custom-written computer program which received data from a digitiser board. Atrial activation points were directly entered from the hard copy recordings of the Atrioversion procedure. The activation time was taken as the peak of a symmetrical bipolar electrogram, or the first rapid deflection of any other electrogram (see Section 4.5.1). Between 3 and 10 flutter beats preceding the impulse are entered; the program calculates the mean and variance of the flutter cycle length. Then S, A2 and subsequent atrial beats are entered.

Using a 95% Student's-t confidence limit, data analysis shows if:

1) The stimulus has captured (A2 advanced).

2) The return cycle is significantly shortened (non-compensatory).

5.4.2 Refractory periods

Refractory periods were measured at 56 atrial sites in 45 cases. Reasons for exclusion of patients were non-measurement of excitable window (3 cases), excessive variation in atrial cycle lengths (9 cases), and obliteration of the A2 signal by the stimulus artifact (21 cases); this latter problem was particularly common early in the series, but increased decoupling on the input of the amplifiers improved the trace quality sufficiently that A2 can now almost always be visualised. The results of the refractory period measurements are shown in Table 5.2.

Thirty nine of the 56 sites were on the lateral wall of the right atrium; 7 high, 18 mid and 14 low. Four sites were high in the anterior right atrium, near the right atrial appendage, 3 were on the mid atrial septum, and 3 were low on the septum. In 7 cases, the site was inadequately visualised, and no anatomic location was recorded.

ERP and FRP are shown as absolute figures and also as a percentage of the flutter cycle length. ERP ranged from 44% to 79%, with a mean value of 59.4% (standard deviation 7.2). The mean value of FRP was 78.7% (standard deviation 7.7); the range was 58% to 94%. Neither ERP nor FRP was significantly different between Type I and Type II atrial sites. There was also no difference in the mean values between the different anatomical atrial sites. Thus the excitable gap, as assessed by the FRP measurements, ranged from 6% to 42% of the cycle length.

TABLE 5.2

ATRIAL FLUTTER

REFRACTORY PERIODS

Case No.	Name	Site	Cycle	Window length	ERP type		FRP	
			ms		ms	%	ms	%
6	HM	MRA	197	1	128	65	143	72
8	WK	MRA	186	2	105	56	165	89
10	LM	RAA	185	1	119	64	162	88
14	JS(1)	MAS	252	2	139	55	145	58
15	JC	MRA	183	2	104	57	154	84
17	TH	MRA	277	2	143	52	172	62
18	NG	MRA	238	2	158	66	178	75
24	MG	MAS	236	2	135	57	207	88
26	RU	MRA	215	2	114	53	155	72
27	EA	MRA	219	1	104	47	145	66
29	CC	LRA	181	2	128	71	162	90
30	AH	LRA	174	2	125	72	156	90
31	NM(2)	RAA	210	1	123	59	146	70
		HRA	222	2	157	71	196	88
32	RM(1)	MRA	216	1	112	52	179	83
		LRA	216	1	126	58	142	66
33	JB(1)	HRA	240	1	144	60	189	79
35	TA	LRA	195	1	115	59	136	70
		HRA	194	2	116	60	138	71
38	JS(2)	?	228	2	150	66	195	86
44	RA	MRA	205	1	121	59	140	68
46	JM	MRA	217	1	125	58	162	75
48	GK	LRA	202	1	142	70	170	84
49	DC	MRA	265	1	180	68	215	81
51	TN	LRA	215	1	135	63	175	81
52	JH	LRA	225	1	140	62	180	80
55	JV	LRA	235	1	129	55	167	71
56	WM	LRA	190	1	90	47	152	80
57	FM	MRA	200	1	105	53	160	80
58	EM	MRA	275	2	130	47	210	76
59	LK	LRA	270	1	170	63	218	81
60	GA	MRA	210	1	142	68	178	85

TABLE 5.2

(continued)

ATRIAL FLUTTER

REFRACTORY PERIODS

Case No.	Name	Site	Cycle	Window length	ERP type		FRP	
			ms		ms	%	ms	%
61	PB	HRA	217	1	119	55	172	79
		LAS	209	1	124	59	161	77
62	HA	HRA	207	1	125	60	148	71
		MRA	205	1	91	44	143	70
63	AS	LRA	239	1	149	62	203	85
64	TS	LRA	220	1	150	68	180	82
65	KO	LRA	187	1	105	56	160	86
66	HM	?	235	2	132	56	175	74
67	AM	?	206	1	135	66	180	87
68	LA	LARA	222	1	120	54	185	83
		MAS	222	1	145	65	205	92
		LRA	222	1	140	63	200	90
69	RG	MRA	226	1	140	62	190	84
		HRA	226	2	140	62	185	82
70	DW	?	308	1	200	65	240	78
		HRA	308	1	165	54	235	76
71	MC	MAS	214	1	110	51	160	75
72	MH	RAA	220	2	125	57	165	75
73	FD	MRA	203	1	160	79	180	89
74	RM(4)	?	243	1	135	56	205	84
75	EM	?	235	1	150	64	220	94
76	TS	LRA	206	1	90	44	155	75
77	WM	?	200	2	120	60	145	73
78	RQ	MAS	298	1	175	59	250	84

Key :
ERP - effective refractory period
FRP - functional refractory period
HRA - high lateral right atrium
MRA - mid lateral right atrium
LRA - low lateral right atrium
MAS - mid atrial septum
LAS - low atrial septum
LARA - low anterior right atrium
RAA - high anterior right atrium
? - anatomical position not recorded

Refractory periods were measured at more than one atrial site in 8 cases. In case 31, measurement was made after conversion of flutter from the common to uncommon form. In the other 7 cases, the flutter form was unchanged before and after catheter repositioning. It can be seen in cases 35, 61, 62, 69 and 70 that FRP is the same, within 3%, for both sites. No dispersion in refractoriness is seen. However, in cases 31, 32 and 78, sites differ in FRP by between 7% and 17% of the cycle length. This non-uniform refractoriness, if also present during sinus rhythm, may play a part in flutter initiation in these patients.

5.4.3 Type of excitable window during flutter

The highest proportion of Type I sites was found in the low anterolateral right atrium, where 14 out of 16 sites showed a Type I response. In comparison, 11 of 17 mid anterolateral, 6 out of 10 high anterolateral, and 4 out of 6 septal sites showed Type I responses. Thus the low anterolateral right atrium seems to be more often important in the mechanism of flutter, whether due to its inclusion in a reentry circuit, or to its proximity to a focus.

5.4.4 Case report

Case 62

Figure 5.10 shows a typical pattern, from case 62, of a refractory period measurement. The first two panels are surface lead II and a bipolar trace from the mid right atrium. Atrial flutter is present, with a cycle length of 210 ms. Stimulation was carried out from two electrodes 1 cm away from the recording electrodes; the activation time was 30 ms earlier than at the recording site, showing the intervening tissue to be an area of slowed conduction. The eleven subsequent panels show a synchronised display of single extrastimuli delivered at increasing prematurity (the value of A1-S is shown at the left edge of each panel). The first ten stimuli all provoke an atrial ectopic. The A1-A2 value is

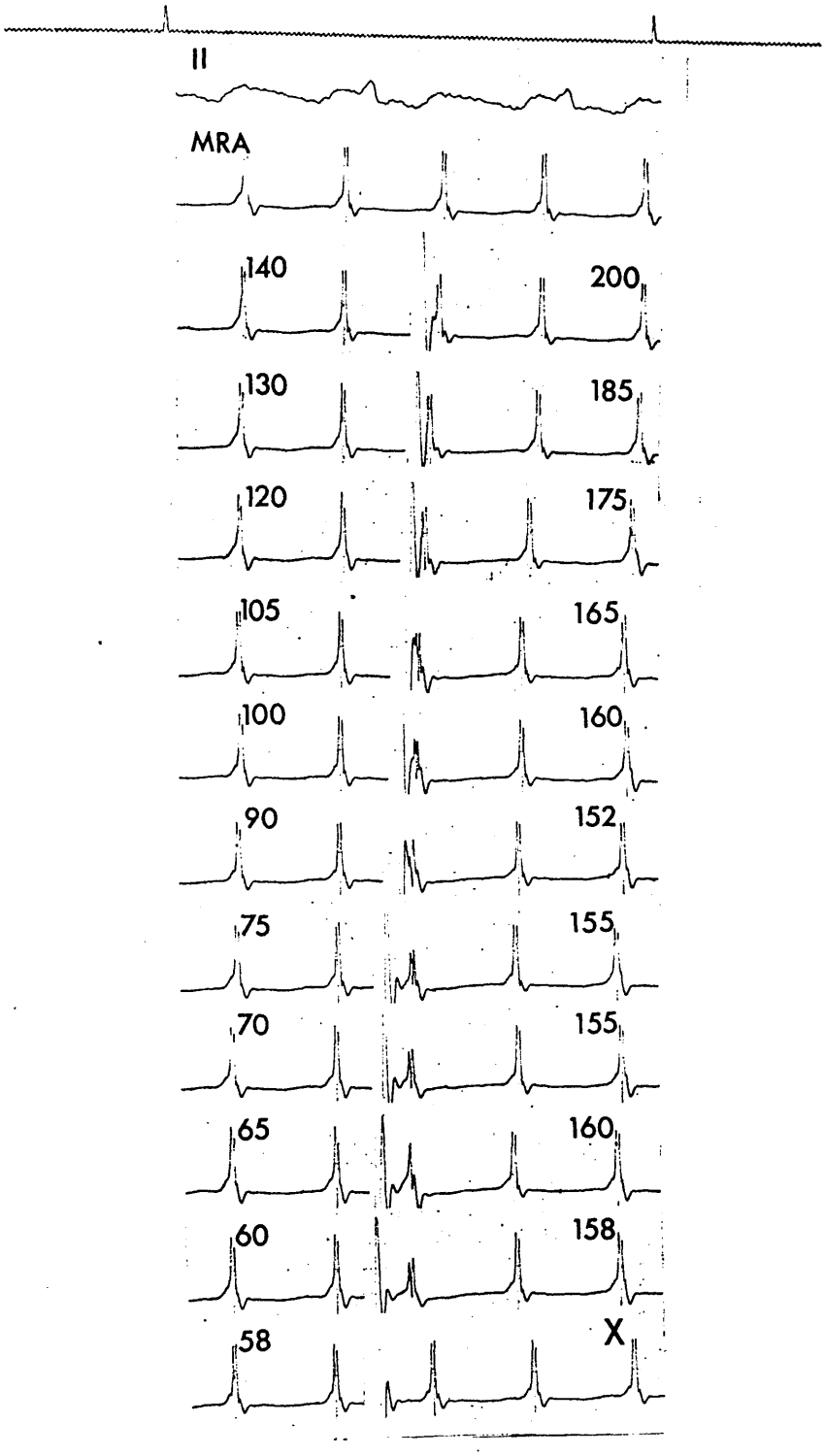


Figure 5.10

Measurement of atrial refractory periods during flutter (cycle length 210 ms). The top 2 panels show surface lead II and a bipolar mid right atrial electrogram. The next 11 panels show stimuli delivered with increasing prematurity, until refractoriness is encountered. A1-S is shown at the left of each panel, and A1-A2 at the right. The shortest A1-A2 is not induced by the most premature stimulus, due to latency of conduction.

at the right of each panel; the 'X' in the final panel denotes loss of capture due to refractoriness. The most premature stimulus which captures is coupled at 60 ms, and this stimulus produces a premature atrial cycle measuring 158 ms. The shortest A1-A2 value, however, is 152 ms, and results from the 6th stimuli, coupled at 90 ms; all stimuli after this are subject to latency, as can be seen by the increasing gap between stimulus and atrial electrogram. The last panel shows that the atrium becomes refractory when the stimulus is coupled at 58 ms. The true value of the effective refractory period at the stimulation site is 30 ms greater, due to its earlier activation. The return cycles all measure between 210 and 220 ms. They are not compensatory, and this is an example of a Type I excitable window. Note that, although the window is 80 ms wide with respect to stimuli, it is only 48 ms wide with respect to atrial response.

In summary, in the present series, there was an excitable gap in 45 cases of atrial flutter and at most atrial sites. The gap averaged 41% of the atrial cycle with respect to applied stimuli (mean effective refractory period 59%). The mean functional refractory period was 78%; thus, on average, atrial sites can be prematurely depolarised by a maximum of 22% of the cycle length during atrial flutter.

5.5 Multiple site measurement of excitable window

5.5.1 Introduction

In Section 5.2.4, it was pointed out that the existence of Type I responses at separate atrial sites differing in activation time is not compatible with the automatic focus theory of atrial flutter. Such results were obtained in 8 patients in our series. These cases are amongst the more recent in the series, partly because early recording quality did not allow satisfactory estimation of evoked atrial response following extrastimuli, as was discussed in Section 7.4, but more importantly because it is often necessary to insert two atrial catheters in order to record from two sites with sufficient separation in activation times.

Insertion of a second catheter has only been carried out fairly recently in this series.

Individual cases will be discussed below.

5.5.2 Case reports

Case 61

Figure 5.11 shows four surface leads and three electrograms from the lateral right atrial wall. The atrial flutter cycle length is 210 ms. A stimulus to the low right atrium produces a response coupled at 170 ms, and the return cycle is not compensatory. If an automatic focus is present, then two conclusions can be drawn:

1) The focus is anatomically close to the low right atrial site.

2) There is a very short conduction time from the focus to the low atrial site.

Stimulation was then carried out in the mid right atrium. Here, atrial activation occurred 70 ms later than low in the atrium, and therefore there must be a long conduction time, of the order of 70 ms, from this site to the focus. Clearly, any stimuli at this second site cannot prematurely depolarise such a distant focus. However, from Figure 5.12, it can be seen that the stimulus does reset the flutter. The cycle length is now 220 ms. The unipolar MRA electrogram is obscured by the artifact, but the high right atrial electrogram, which is 10 ms later, clearly shows a non-compensatory pause following a short premature cycle. This result is incompatible with a discrete focus of activity, whether due to enhanced automaticity or micro-reentry, and it must be concluded that a macro-reentry circuit is present in this case of

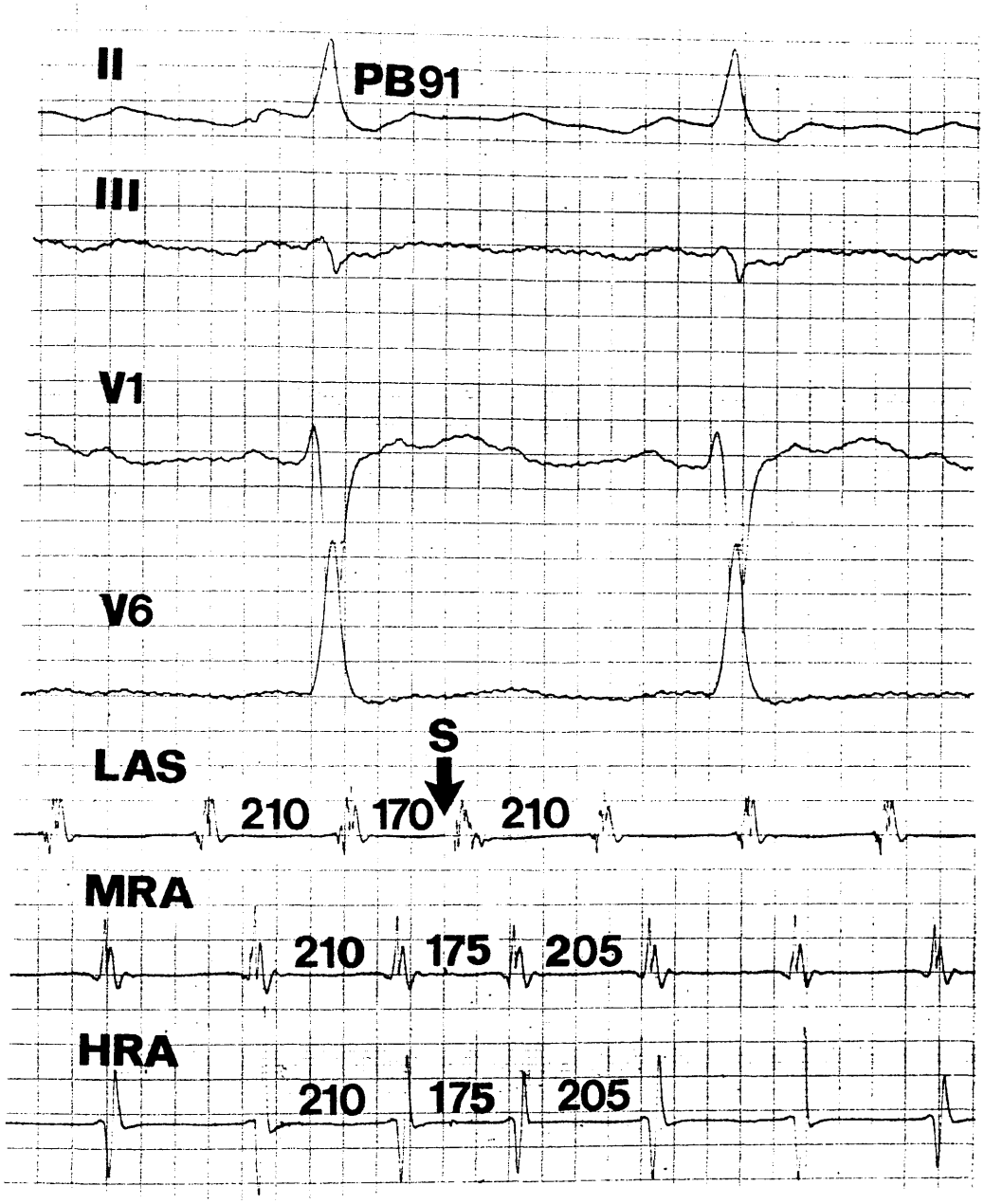


Figure 5.11

Case 61. A Type I response is seen following stimulation of the low atrial septum. Reset is also seen in the mid and high lateral right atrium.

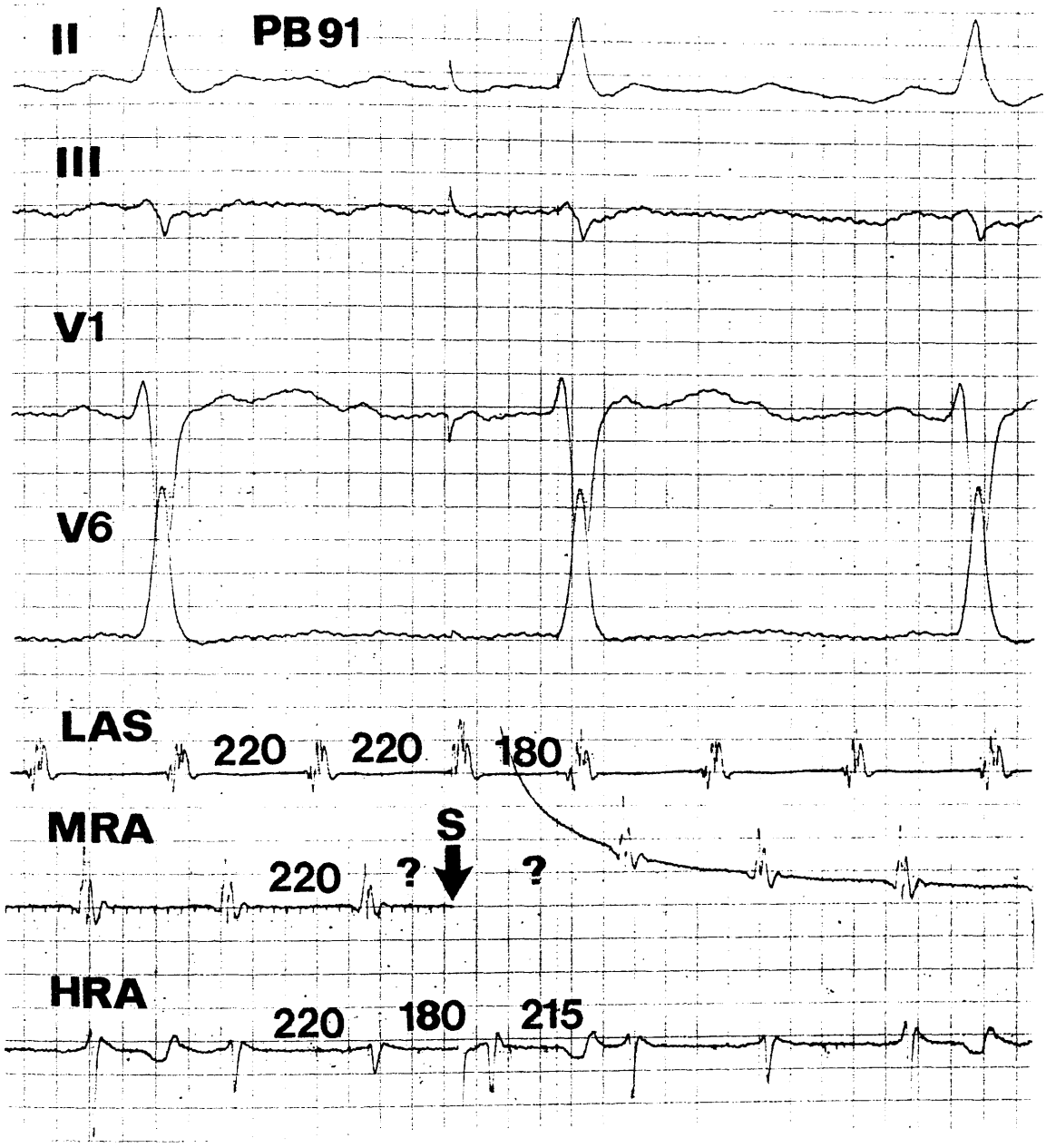


Figure 5.12

A Type I response is again seen in Case 61 in the mid lateral right atrium. Activation at this site is 70 ms later than low septum (see Figure 5.11). The septal trace shows reset in the cycle after that enclosing the stimulus.

atrial flutter. Further support comes from examination of the low right atrial electrogram in Figure 5.12. The cycle which encompasses the stimulus is not shortened by that stimulus. Since LRA is depolarised before MRA, then if a focus was present, it presumably had not been affected. However, the next cycle, which does not include the stimulus, is markedly shortened by that stimulus. Hence it can be concluded in this case that access to the origin of the flutter can be gained from a different site spatially and temporally apart. The low and mid right atrial sites were separated by approximately 2 cm (estimated from X-ray screening). The high right atrial site, a further 2 cm away, showed a Type II response, with long return cycles. Thus, a reentry circuit has been found involving some, but not all, of the lateral wall of the right atrium.

Case 62

Figures 5.13 and 5.14 are from case 62. Again, three atrial electrograms are shown. In Figure 5.13, stimulation of the high right atrium produces a premature cycle of 155 ms and a short return cycle of 215 ms - a Type I response. The mid right atrial electrogram confirms these figures. The cycle length is 210 ms, so a return cycle of 215 ms implies that the conduction time to circuit or focus is less than 3 ms. Activation of the mid right atrium is 30 ms later, so the minimum conduction time to a focus from here must be 27ms. The minimum return cycle possible after mid right atrial stimulation is therefore 210 + 2 x 27 ms, or 264 ms. In Figure 5.14, a stimulus to the mid right atrium evokes a response at 170 ms (deduced from high right atrial trace). The return cycle is 215 ms, and again the flutter is reset. As with case 61, these findings are not compatible with an automatic focus, but can only be explained by a macro-reentry circuit.

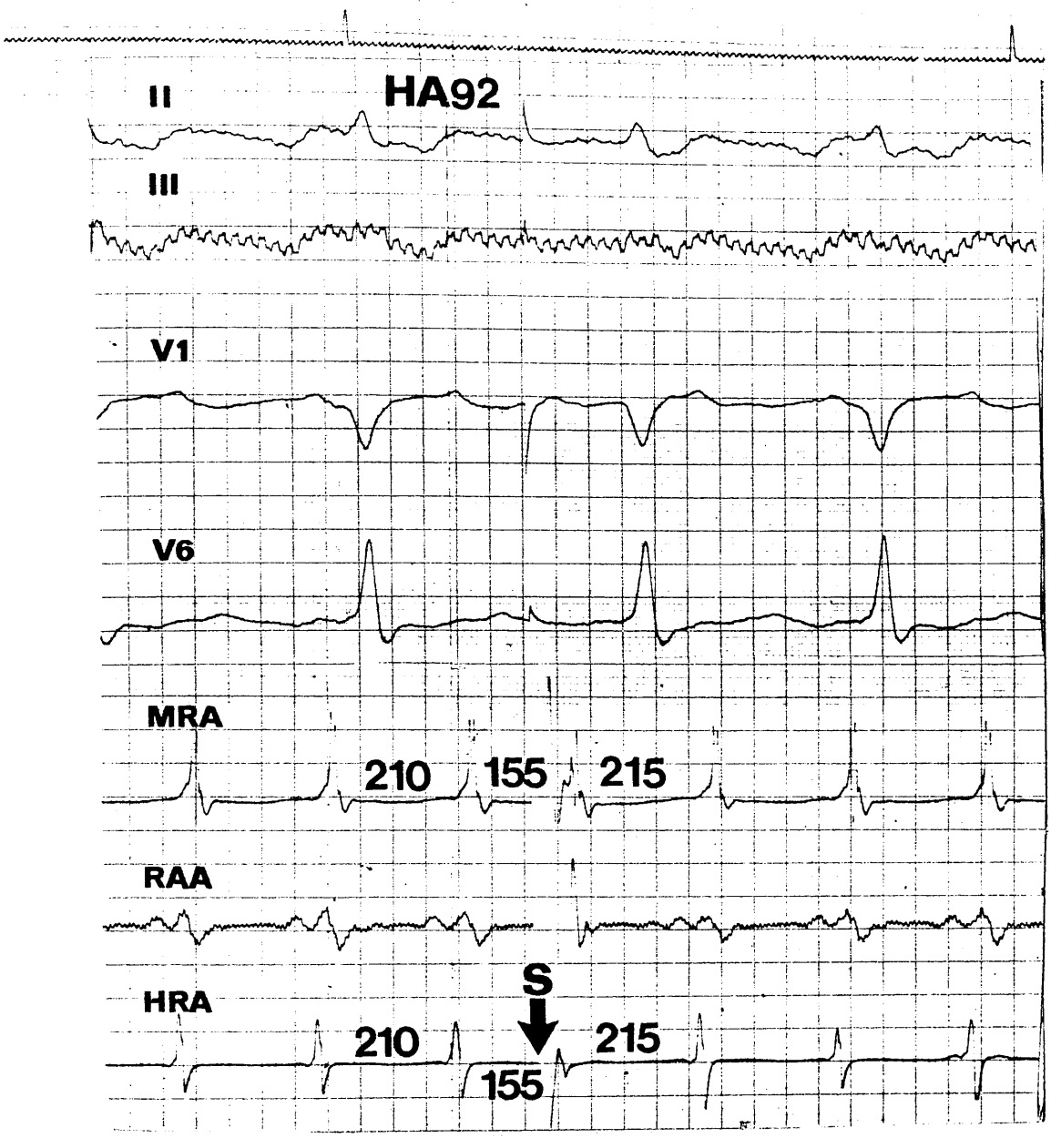


Figure 5.13

Case 62. Type I response in the high lateral right atrium.

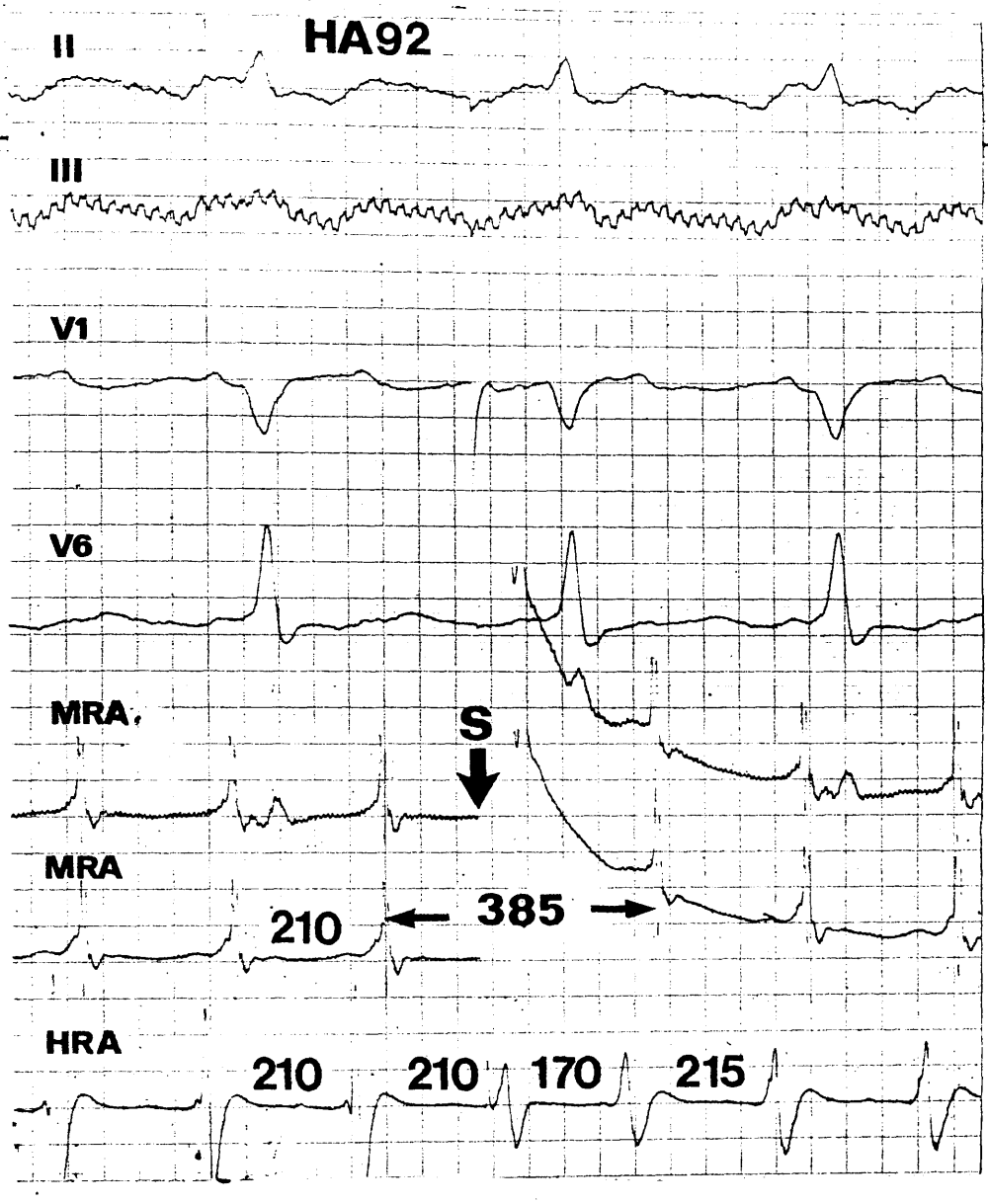


Figure 5.14

Case 62. Mid right atrium is activated 40 ms after high right atrium. A Type I response is again seen.

Case 41

Figures 5.15 and 5.16 show the results of extrastimulation at two sites in case 41. In Figure 5.15, the return cycle following mid right atrial stimulation is 215 ms, and does not exceed the flutter cycle. Activation at the stimulating electrodes coincided with the first (slower) deflection in the MRA trace, as marked. Low right atrial activation (Figure 5.16) is 90 ms after the first deflection in the MRA trace. The return cycle here is also not compensatory, although prolonged by 20 ms. The flutter is reset by 45 ms, which is again incompatible with a focus.

Case 68

Figure 5.17 shows atrial stimulation at three sites in this case (see also endocardial map below). The left panel shows a Type I response in the low anterior RA, with a reset of 35 ms after a stimulus S, seen in all three electrograms. The middle panel again shows a Type I response at the mid septal site (MAS). This site is activated 70 ms after the low anterior site. Finally, the left panel shows reset at the low anterolateral RA, a site activated 70 ms after MAS and 140 ms after the low anterior site. These activation times are spread equally throughout tyhe cycle, and the only explanation for all 3 showing a Type I response is that all 3 are included in a macro reentry circuit.

The above results were also reproduced at double sites in cases 63, 64, 65 and 78..

5.6 Endocardial mapping of atrial flutter

5.6.1 Introduction

Atrial endocardial electrograms were recorded during atrial flutter in all patients. Early in the series careful estimation of the catheter's anatomic position was not routine, but in later cases, multiple sites were commonly mapped.

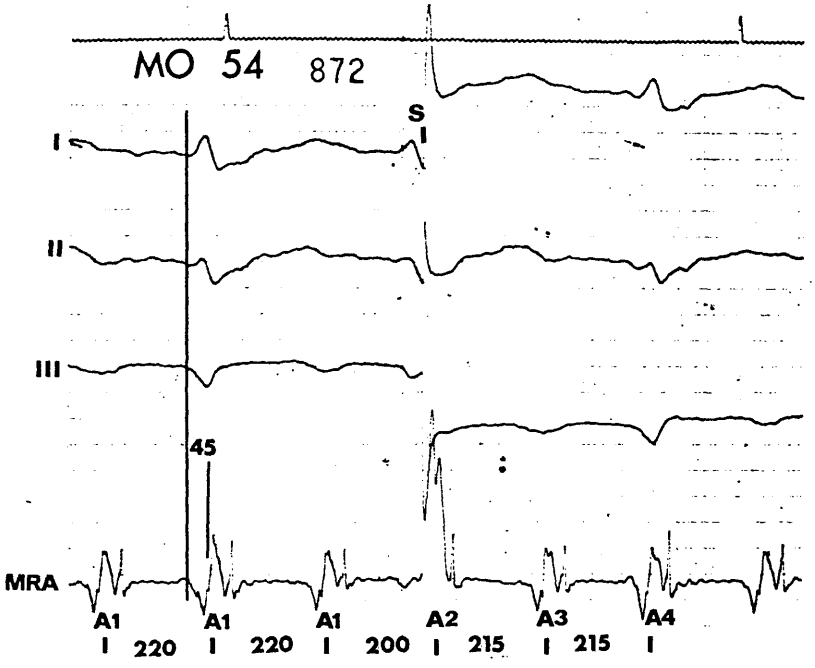


Figure 5.15

Case 41. Type I response in mid lateral right atrium.

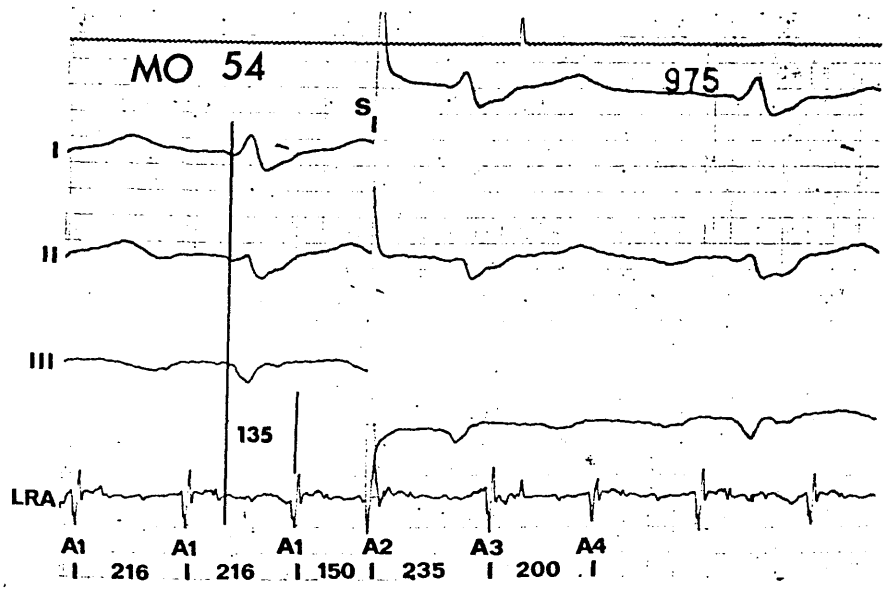


Figure 5.16

Case 41. Low right atrium is activated 90 ms after mid right atrium. A Type I response is seen. Return cycle is prolonged, but not compensatory.

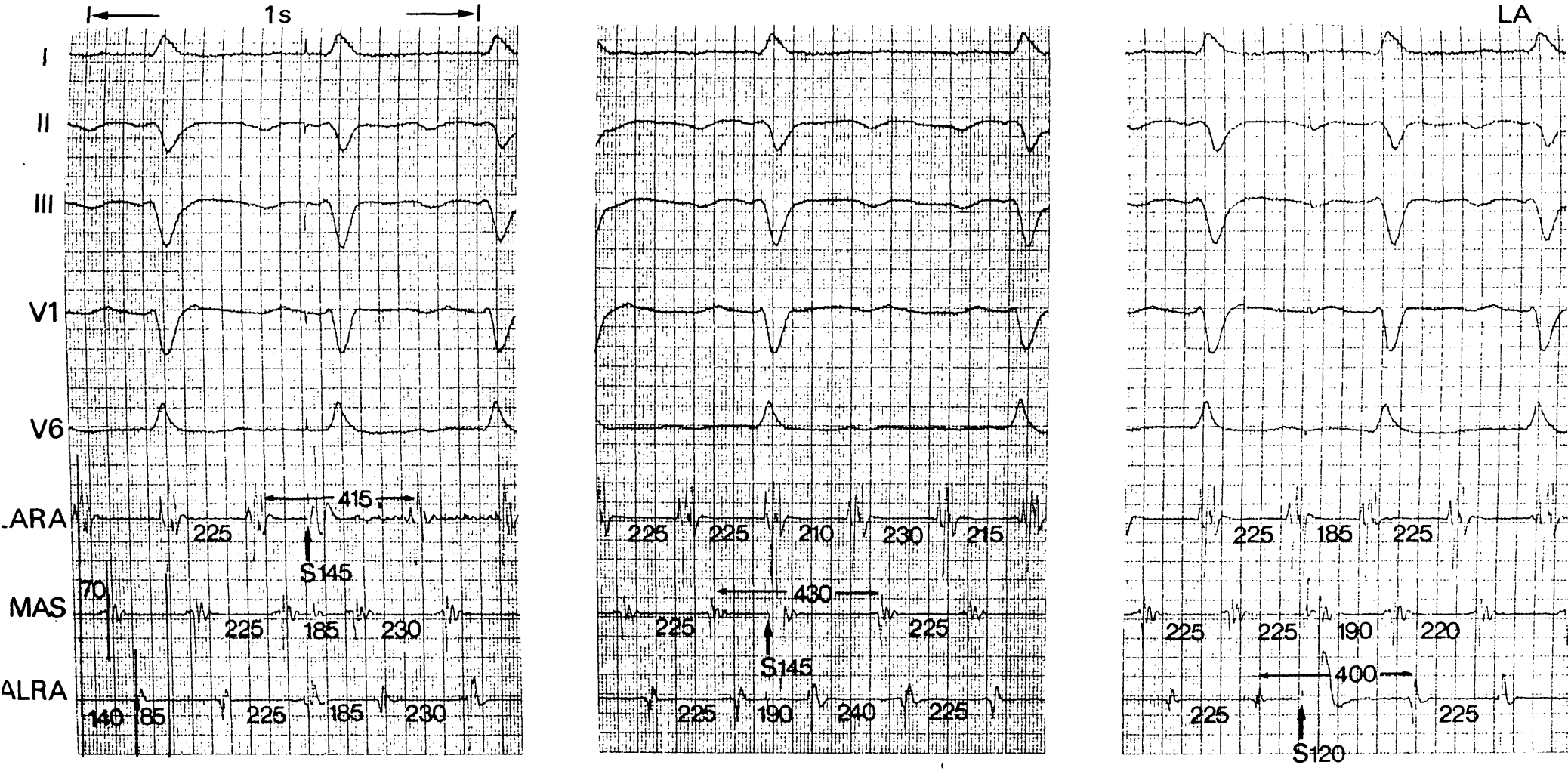


Figure 5.17

Case 68. Type I responses are shown at 3 sites - left panel : low anterior right atrium (LARA), centre panel : mid atrial septum (MAS), and right panel : low anterolateral right atrium (LALRA). Activation at these sites spans 140 ms of the flutter cycle of 225 ms.

In 54 cases, 1 to 13 atrial electrograms were recorded from identifiable atrial sites. In total, 250 electrograms were obtained (average 4.3 per case).

In 46 cases, flutter was of the common type, in 5 cases the uncommon type was present, and in 3, no surface flutter waves could be seen.

Anatomical sites were divided into four groups:

1) Right atrial anterior wall
2) Right atrial lateral wall
3) Inter-atrial septum
4) Coronary sinus

Electrograms were recordable from five sites ranging from high to low in each of the first three categories above, and from proximal to distal coronary sinus. Lateral wall sites (160) were the most commonly recorded. These sites are the most easily accessible to catheter manipulation. Other sites recorded were the interatrial septum (39 sites), anterior right atrium (42 sites) and coronary sinus (9 sites) Figures 5.18 and 5.19 show a summary of the overall mapping results in all cases. In Figure 5.19, median activation times are shown at sites where at least 5 electrograms were recorded. The zero reference point is the nadir of the flutter wave in leads II and III for common flutter, or the peak for uncommon flutter. The anterior and lateral walls are activated during the first half of the flutter cycle, and the septal wall during the second half. In addition, the lateral wall is activated downwards.

5.6.2 Mapping of common atrial flutter

Mapping of 220 sites in the 46 cases of common atrial flutter did not reveal a consistent pattern of atrial activation. Three or more electrograms from the lateral wall were obtained in 35 cases. A consistent downwards spread of

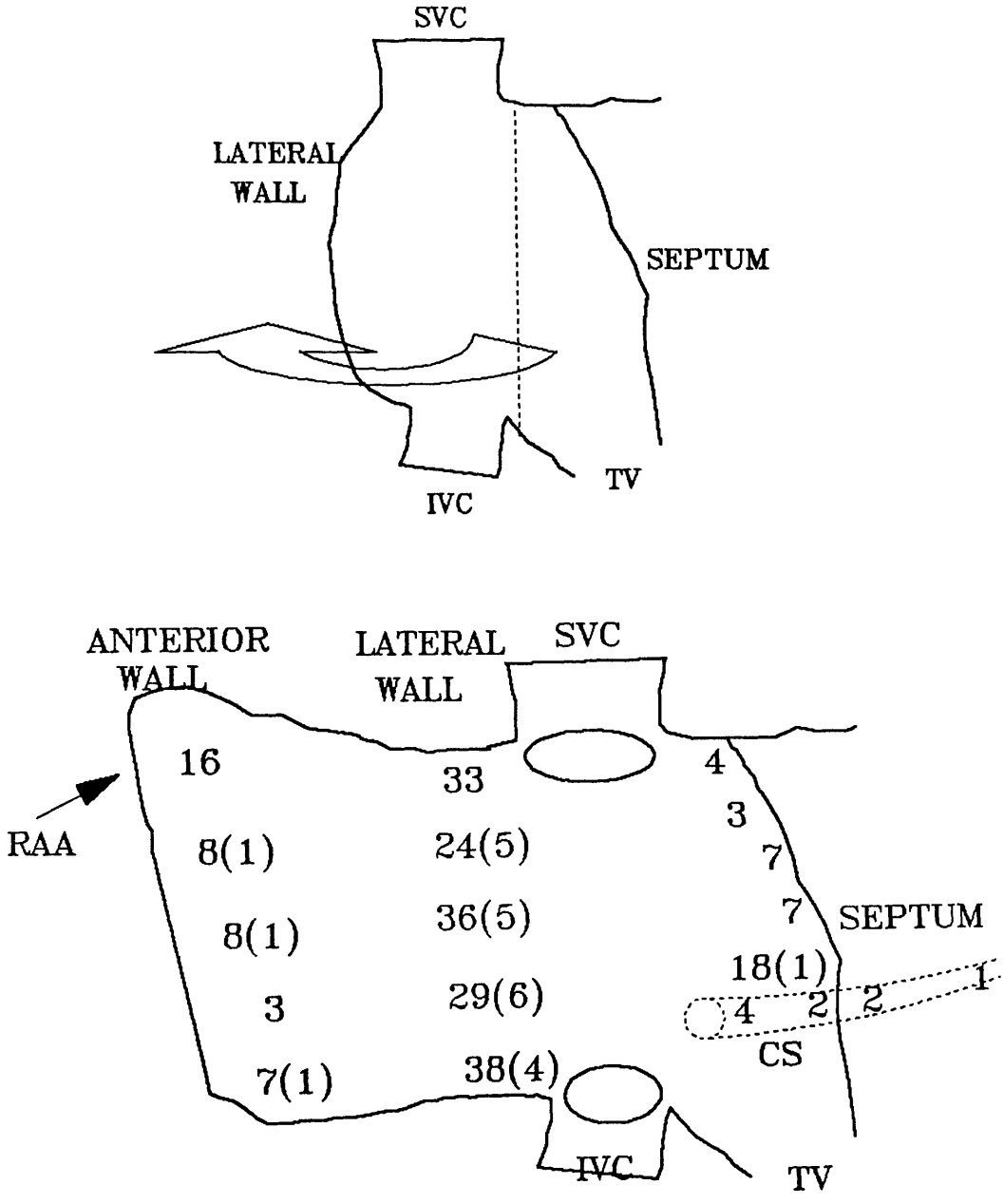


Figure 5.18

Endocardial mapping of atrial flutter in 53 cases. The upper panel shows the anterior view of the right atrium. For display purposes, the atrium is "opened out" along the anteromedial line (shown dotted). The lower panel shows the total number of electrograms obtained from each site (number of split electrograms in brackets).

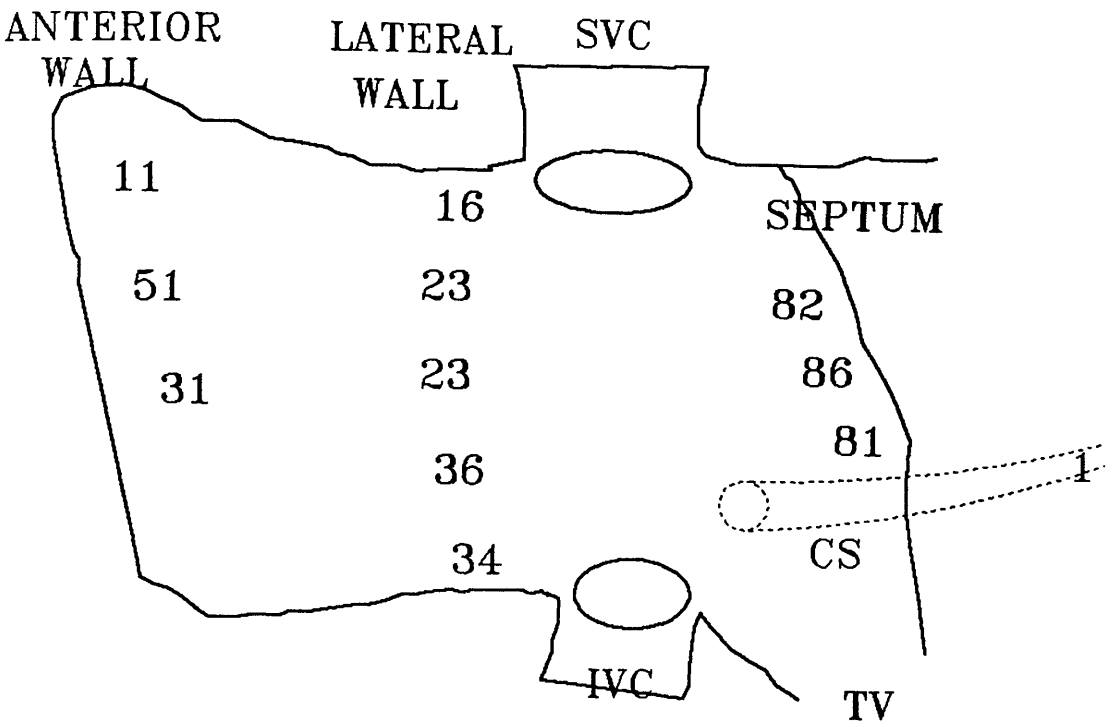


Figure 5.19

Endocardial activation during atrial flutter.
Median time of activation, expressed as a % of the flutter cycle length. Only sites with at least 5 recorded electrograms have been included.
The anterolateral right atrium is activated during the first half of the flutter cycle. The septum is activated late in the cycle. Zero reference is the nadir of the flutter wave in the inferior ECG leads (II and III).

activation could be identified in 20 cases. Upwards activation was seen in 3 cases, and in 12 activation was not consistently in either direction.

The inter-atrial septum could be mapped in 8 cases. In 7, activation was upwards (lateral wall downwards in 4, upwards in 1 and indeterminate in 2); in 1, activation was downwards, as was lateral wall activation. Thus in 4 out of 7 cases, the lateral wall was activated in the opposite direction to the right atrial surface of the septum, and in 2 cases was activated in the same direction.

In the 3 cases where a coronary sinus catheter was introduced, activation spread from the distal coronary sinus towards the right atrium. Distal coronary sinus activation preceded high right atrial activation by 50 to 90 ms. It should be remembered that if atrial flutter is a circus movement tachycardia (as this study has suggested), and activation is continuous throughout the flutter cycle, then the term "preceded", which implies a fixed zero time reference point, becomes difficult to interpret.

Split potentials have been advanced as a marker of slow conduction and/or reentry (Cosio, 1986). Overtly split potentials were seen at 19 out of 220 sites (8.6%) during the common form of atrial flutter. These were predominantly found in the mid-lateral (6) or the low lateral (9) right atrium. Two were found on the mid/low anterior right atrium, and 1 at the low septal right atrium.

Three individual endocardial maps will be discussed in detail.

Case 61

Figure 5.20 shows the activation pattern in case 61. Atrial flutter of the common type is seen in the surface leads. Ten intra-atrial electrograms are displayed; these were not recorded simultaneously, but have been time-synchronised by using their fixed relationship with the surface ECG. The black line is drawn arbitrarily before the distal coronary sinus electrogram, to

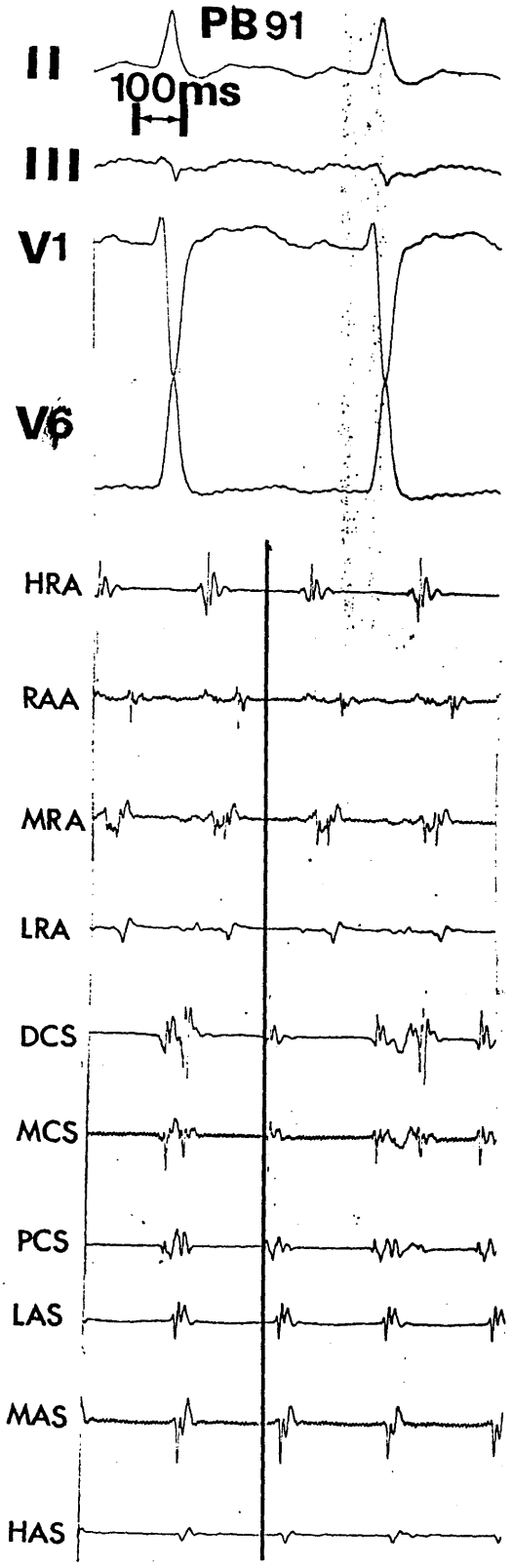


Figure 5.20

Endocardial mapping of atrial flutter in Case 61. Four surface leads and 10 atrial electrograms are shown. The flutter cycle length is 210 ms. See text for discussion.

help visualise the activation pattern. Activation spreads from distal coronary sinus towards the right atrium, and then up the septum (DCS to PCS to HAS). It then proceeds down the lateral right atrial wall. Latest activation (relative to DCS) is seen in the right atrial appendage (RAA). In this case, activation of atrial myocardium is recorded over 145 ms of the 210 ms flutter cycle. Such limited numbers of electrograms are unlikely to show a wider span of activation, or to demonstrate a localised circus movement (Allessie, 1984).

Case 59

A slow atrial flutter is present (Figure 5.21). Seven electrograms from progressively lower positions on the right lateral wall are shown. Activation becomes progressively earlier until the fifth electrogram, then in the lower traces the activation is much later in the cycle. The line drawn relates the electrograms to the nadir of the flutter wave in lead II. The figures are in ms. In the fifth electrogram, two low amplitude deflections are seen, with the deflections separated by 115 ms - almost half of the cycle length. This may indicate an area of block, as demonstrated in the experiments of Allessie (1977, 1984). Thus activation is seen to be basically upwards in the lateral wall, but there is a discontinuity of 100 ms in the low/mid right atrium.

Case 68

Figure 5.22 shows the map of 5 surface and 10 endocardial electrograms in this patient. The atrial flutter cycle length is 220 ms. An arbitrary zero line has been drawn at the onset of the flutter wave in leads II and III. Activation appears to spread down the lateral right atrial wall, and there is overt splitting of the low lateral electrogram. Mapping was then continued around the anterior tricuspid valve ring (low RA lateral -> septal), and shows progressively later activation. Finally, the mid septal site is activated later than the low septum, suggesting upward activation of the septum. The total

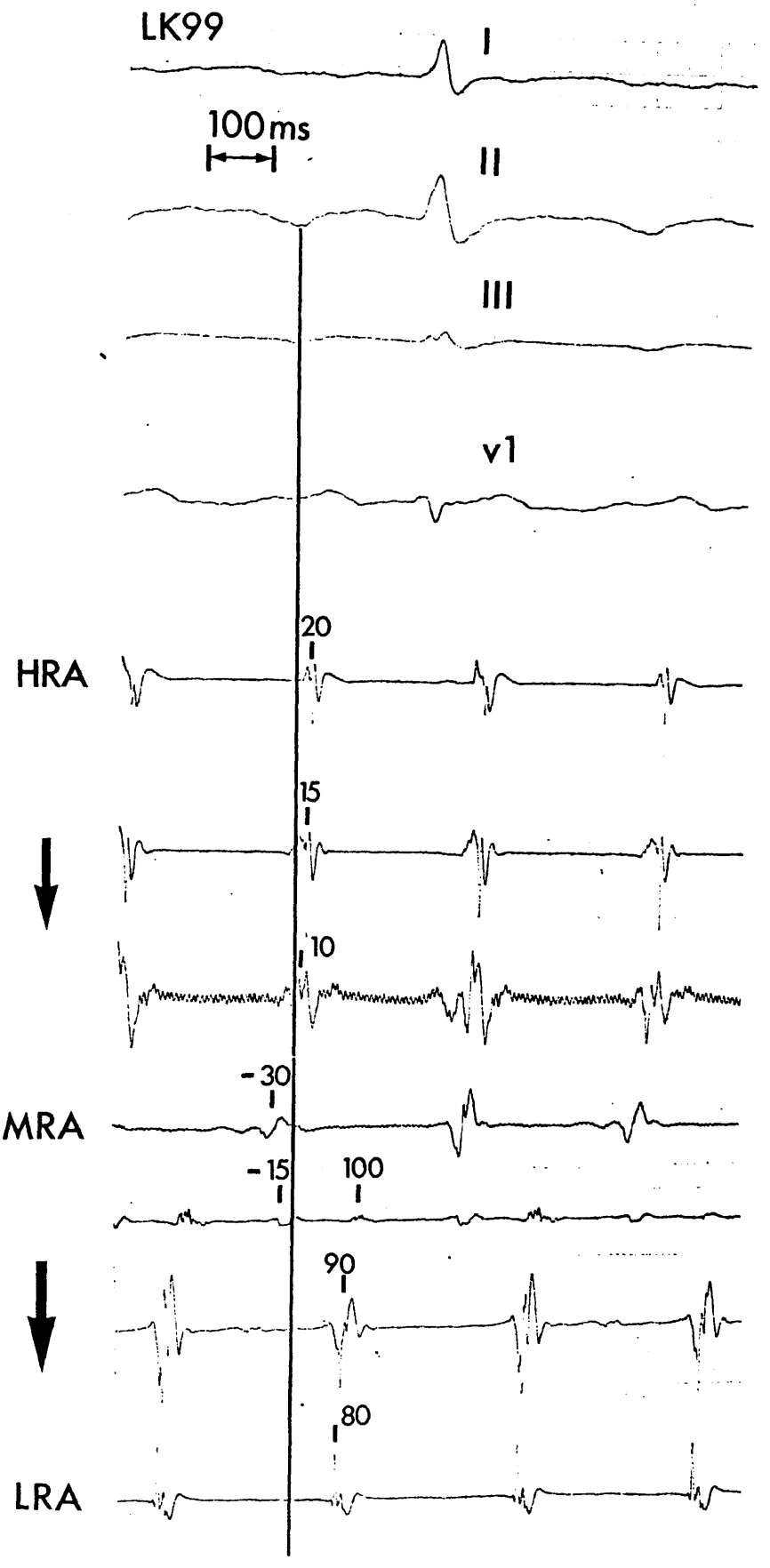


Figure 5.21

Mapping of the right atrial lateral wall in case 59. Four surface leads and 7 electrograms from the right atrial lateral wall. The flutter cycle length is 280 ms.

activation time spanned by these electrograms covers more than one flutter cycle, and therefore not all of these sites can be included in the reentry circuit.

For further clarification, this data should be combined with the discussion of atrial stimulation in this patient (section 5.5.2), where Type I responses were found at the high lateral, low anterolateral and right atrial appendage sites. Activation of these sites spans 150 ms, or 70% of the flutter cycle, and the conclusion must be drawn that macro reentry is occurring in this case.

5.6.3 Mapping of other forms of flutter

Three or more lateral wall electrograms were obtained in 3 of the 5 cases of uncommon flutter. None showed any ordered direction of activation.

Consistent mapping data was obtained on 1 of the 4 cases who showed no visible flutter waves on the surface ECG, and showed downwards activation of the anterolateral right atrium.

5.7 Summary

Atrial stimulation at 56 sites in 45 cases showed that an excitable gap does exist in both common and uncommon forms of flutter, and averages 22% of the atrial cycle length (as assessed by measurement of functional refractory period).

Atrial activation mapping during atrial flutter may not demonstrate conclusively the mechanism of the arrhythmia, but it may be helpful. Endocardial mapping was carried out in 54 cases, and a consistent overall pattern of activation was not found. However, in the majority of cases of common flutter, the lateral wall was activated downwards (so-called cranio-caudal direction).

On 8 occasions, atrial stimulation converted the common form of flutter to the uncommon form, or vice versa, with similar atrial rates but different surface

flutter wave morphology. This finding suggests that the mechanism of the two forms of flutter is the same, and supports macro reentry as the likeliest explanation.

It has been shown in a further 8 cases of common atrial flutter that non-compensatory pauses can be obtained when stimulating at more than one atrial site. In addition, the activation times of these atrial sites differed by a sufficient amount that the observed resetting of the flutter **was incompatible with an underlying automatic focus or micro-reentry circuit.**

It is concluded that a macro-reentry circuit existed in these cases of flutter, with a radius of the order of centimetres, and capable of being explored by a catheter electrode, and stimulated electrically at different points in the circuit. It has also been shown that the axis of the surface P-wave, and the local spread of endocardial atrial activation, can sometimes be altered by an induced atrial premature beat. It is unlikely that this phenomenon could occur in the presence of focal activity.

It is feasible that without the restriction on possible mapping sites imposed by endocardial catheter techniques, Type I responses could be found in all patients at multiple sites. There are obvious limitations when performing only right atrial mapping and stimulation, but nevertheless Type I responses can be found in the right atrium in the majority of cases.

The exact size of the reentry circuit in atrial flutter cannot be concluded from this study, but it appears not to be microscopic. The pathway seems often to include the low and mid antero-lateral right atrium, and sites low on the interatrial septum, but less often the high right atrium, either lateral or anterior. It may be that there is no fixed pathway, and that, despite the apparent similarity of the "common" form of atrial flutter in different patients, the circuit may not lie anatomically in the same place.

Chapter 6

RESULTS - ATRIAL FLUTTER

6.1 Patients

6.1.1 Selection

Conversion of rhythm was attempted in 78 cases of atrial flutter. In 66 patients (50 male, 16 female), one episode of atrial flutter was treated. In 4 patients (2 male, 2 female), there were two episodes, and in one male patient conversion was attempted 4 times. In total, 71 patients were treated, of whom 53 were male and 18 female. There were 78 Atrioversion procedures, 58 on male patients, and 20 on female patients.

6.1.2 Age and sex

The age of the patients varied from 18 to 79 years, with a mean of 54.0 years (standard deviation 13.6 years). The distribution of cases against age is shown in Figure 6.1. The mean age of the male patients was 55.3, and of the female patients 50.2 (not significantly different). There were no significant differences between male and female patients with respect to atrial or ventricular rates, duration of flutter or use of digoxin.

Apart from case 53, when atrial flutter began spontaneously 10 minutes after previously being converted, all repeat cases involved separate hospital admissions and catheterisation procedures.

6.1.3 Surface ECG morphology

Atrial flutter occurred spontaneously in all cases. In 62 patients (69 cases), atrial flutter was initially of the "common" type, with predominantly negative flutter waves in the inferior surface ECG leads (see Figure 4.1), and in 5 patients, the "uncommon" form was present, with positive P-waves in leads I, II and III (Figure 4.2). In 4 patients, no F-waves were visible on the surface ECG.

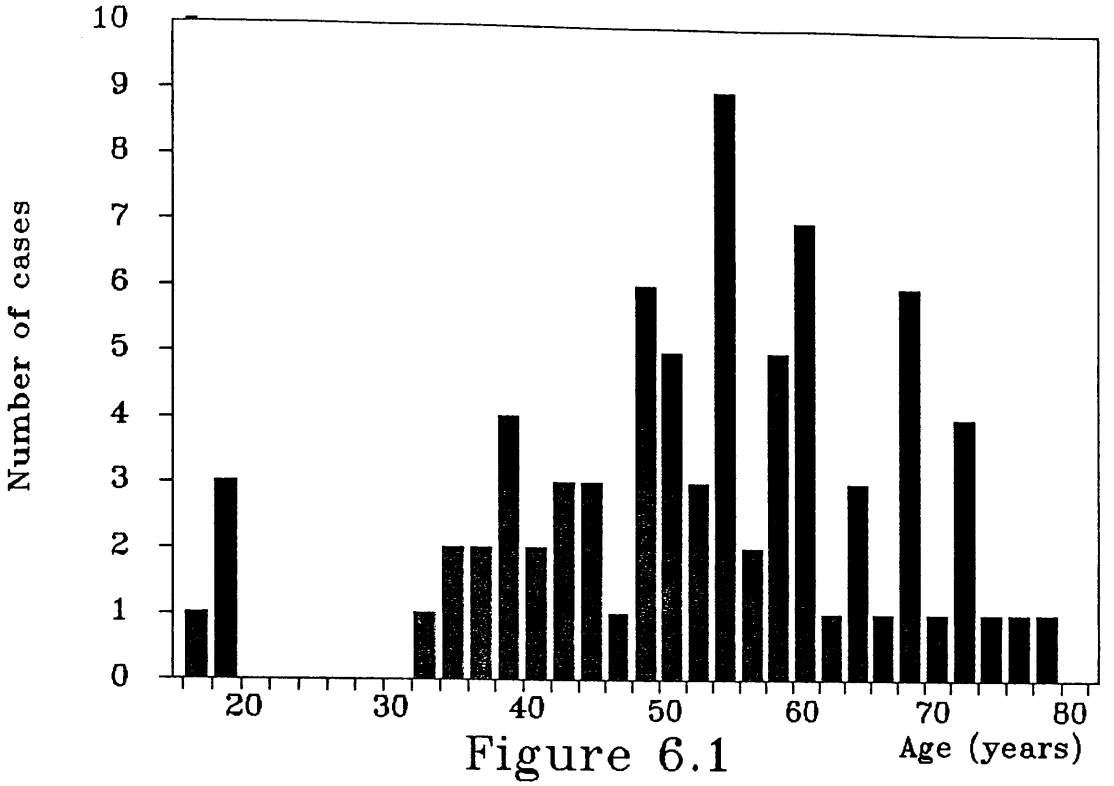


Figure 6.1

The distribution of cases against age.

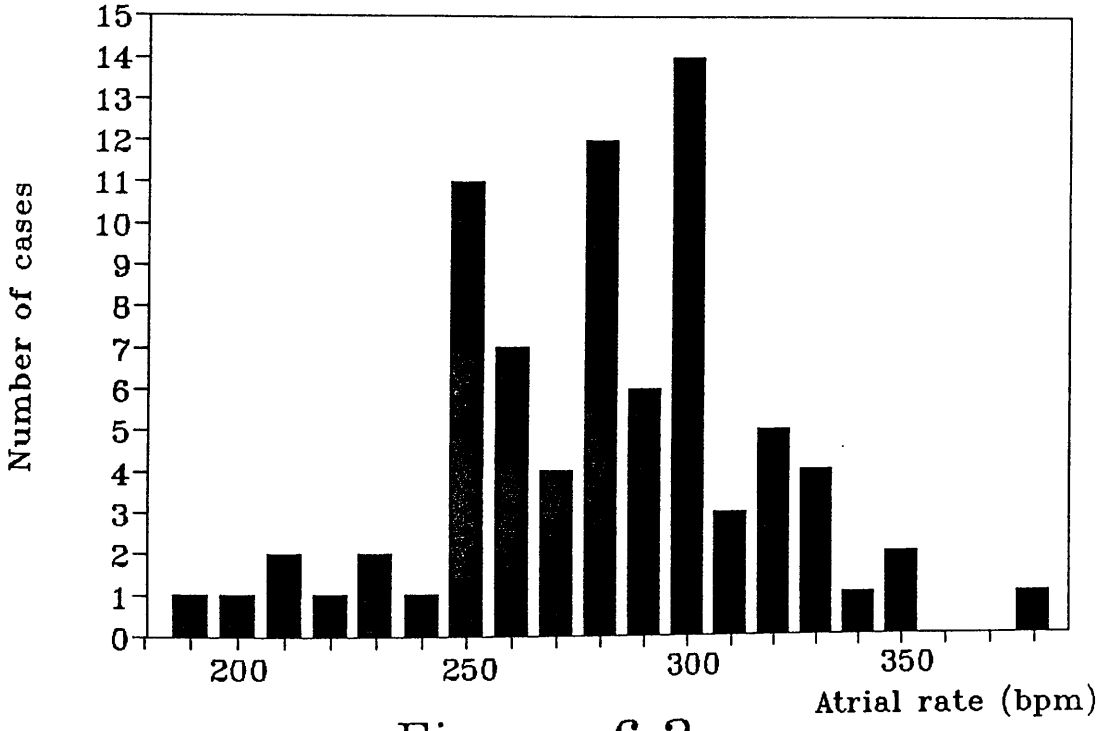


Figure 6.2

Distribution of atrial rates.

(Class interval of x bpm includes rates from x−4 to x+5)

As was discussed in Chapter 5, the common form was converted to the uncommon form in a number of patients, by extrastimuli and/or Atrioversion.

6.1.4 Atrial rate during flutter

The atrial rates ranged from 195 to 380 beats per minute, with a mean of 283, and standard deviation 35. The distribution of atrial rates is shown in Figure 6.2.

2:1 atrioventricular (AV) block was seen in 46 cases, 4:1 AV block in 6 cases, and in the remaining 26 cases, AV conduction was irregular. The mean ventricular rate was 128 beats per minute.

In all but one patient, the ventricular response was less than 1:1. This patient (case 57) was a 40 year old, grossly obese (body weight > 140 kg) man, who was found on admission to be in 1:1 atrial flutter on no therapy, with a ventricular rate of 300 beats per minute (Figure 6.3). He had tolerated this rate well for 6 hours, was well perfused and showed no signs of cardiac failure. Bolus injection of 10 mg verapamil in the Accident/Emergency Department caused 2:1 AV block to supervene, and his ventricular rate fell to 150 beats per minute, which was the rate during the Atrioversion procedure. He was converted to atrial fibrillation, and returned spontaneously to sinus rhythm after several hours. His sinus rhythm electrocardiogram showed a narrow QRS complex and normal PR interval, and his rapid ventricular response during atrial flutter remains unexplained.

6.1.5 Duration of atrial flutter

Duration of flutter prior to Atrioversion is shown in Figure 6.4, on a logarithmic time scale. The median duration was 5 days.

The duration of flutter was greater than 24 hours in all but 3 cases (cases 52, 53 and 57). In case 52, the patient developed atrial flutter during pacemaker insertion for control of bradycardias associated with sick sinus syndrome, and

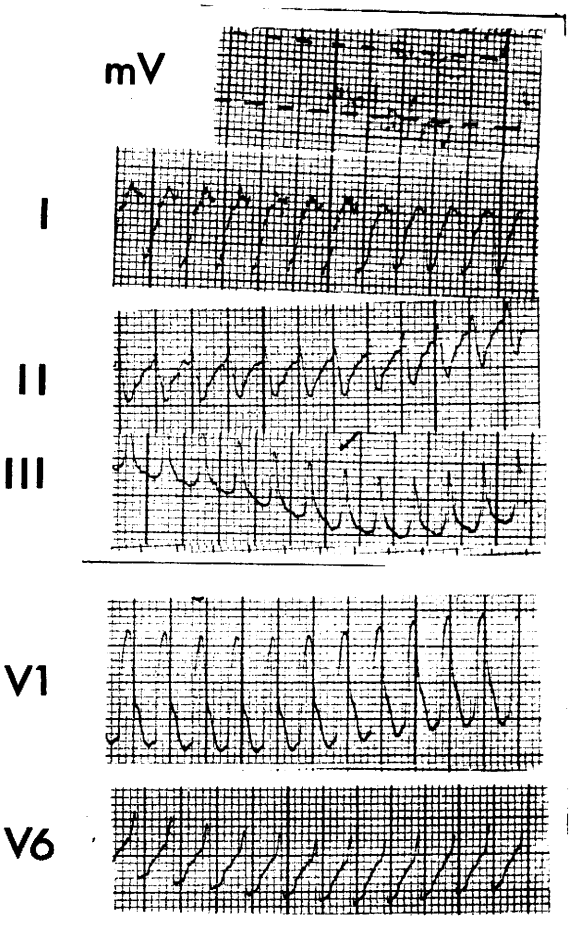


Figure 6.3

Case 57. Atrial flutter with 1:1 ventricular response, rate 300 bpm. 2:1 A-V block developed following 5 mg intravenous verapamil.

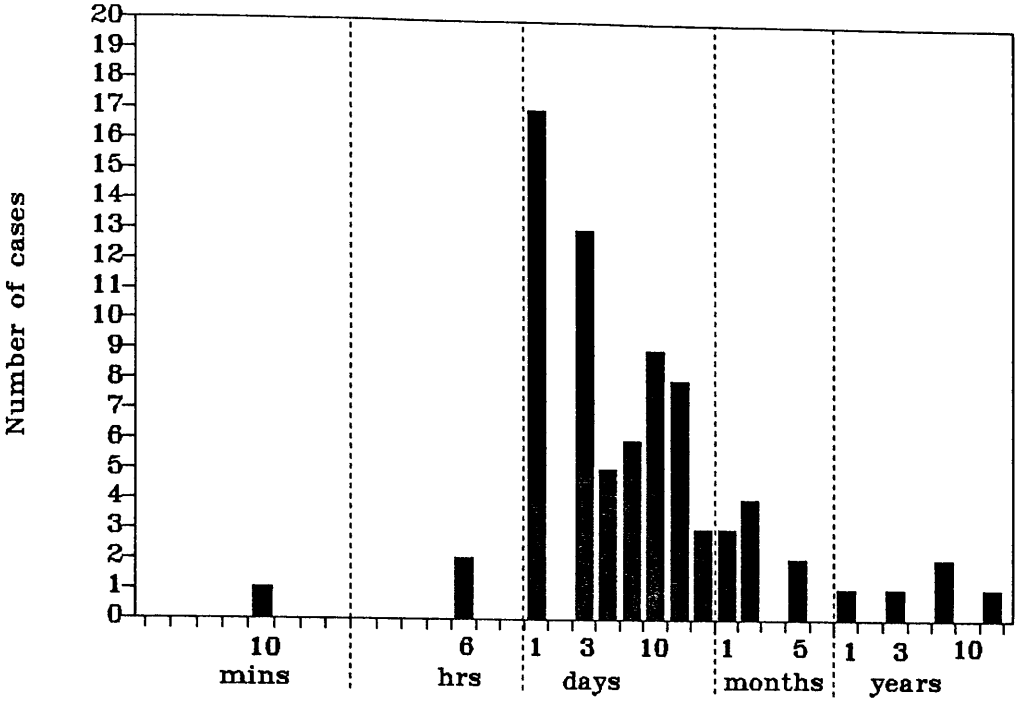


Figure 6.4

Duration of atrial flutter prior to Atrioversion.

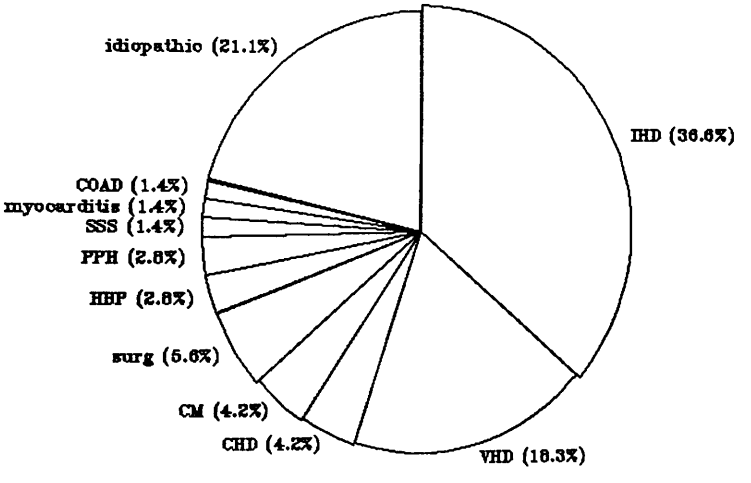


Figure 6.5

Aetiology underlying atrial flutter.

IHD – ischaemic heart disease

VHD – valvular heart disease

CHD – congenital heart disease

CM – cardiomyopathy

surg – non cardiac surgery

HBP – systemic hypertension

PPH – primary pulmonary hypertension

myoc – myocarditis

COAD – chronic obstructive airways disease

SSS – sick sinus syndrome

conversion was attempted 6 hours after flutter began. Case 53 was the same patient, who again developed flutter 10 minutes after conversion, and case 57 was the previously described case of flutter with 1:1 A-V conduction. In 5 patients, the duration of flutter was one year or more.

The relatively long duration in most patients demonstrates that atrial flutter is haemodynamically well tolerated in the short to medium term.

6.1.6 Digoxin

Thirty patients were receiving therapeutic doses of digoxin at the time of Atrioversion. In the remaining 48 cases, digoxin was not used, or was stopped for at least 24 hours prior to Atrioversion.

Remarkably, the only significant difference between digitalised and undigitalised cases was age; the digitalised patients were significantly older. The mean atrial and ventricular rates of the digitalised group (280 and 121 bpm) were not different from the undigitalised group (285 and 133 bpm). This demonstrates that digoxin's reduction of ventricular rate during flutter was very weak or absent in this series.

6.1.7 Aetiology of flutter

The different aetiologies underlying the 78 cases of atrial flutter in 71 patients are shown in Figure 6.5. The most common underlying problem was ischaemic heart disease, in 26 patients. In 2 of these patients, atrial flutter followed acute myocardial infarction, and in 11 of the remaining 24, atrial flutter occurred between 2 and 14 days after coronary artery bypass grafting. In one patient, the ischaemic heart disease was complicated by the presence of sick sinus syndrome. None of these patients has required a repeat conversion.

Valvular heart disease was identified in 13 patients (16 cases). Six of these patients had undergone mitral valve replacement, and 2 had had aortic valve replacements, including the patient who underwent 4 conversions. In contrast

to post-bypass graft patients, no valvular disease patient developed flutter within one month of surgery.

In 3 patients (4 cases), congenital heart disease was the underlying problem. These patients had all undergone corrective surgery, in childhood, for closure of atrial septal defects. Not surprisingly, these patients were amongst the youngest in the Atrioversion series (18, 20 and 33 years of age).

Cardiomyopathy was the diagnosis in 3 patients (4 cases). In 2 patients (3 cases), a hypertrophic cardiomyopathy was present, and in one, a dilated cardiomyopathy developed secondary to hypertension and polyarteritis/vasculitis. Other aetiologies included 4 patients who developed flutter following non-cardiac surgery (3 abdominal, 1 thoracic), 2 patients with systemic hypertension, 2 patients with primary pulmonary hypertension, 1 patient (2 cases) with sick sinus syndrome, 1 with myocarditis, and 1 with chronic obstructive airways disease. In 15 patients (16 cases), investigation revealed no apparent cause, and atrial flutter was labelled idiopathic.

The clinical data on all 78 cases is shown in Table 6.1, and the individual results of electrical conversion in Table 6.2.

6.2 Results using conventional extrastimuli

Table 6.3 shows the results of using a conventional protocol of single, paired and triple extrastimuli (see Chapter 4). Conversion of atrial flutter was achieved in 14 out of 78 cases. On 11 occasions, sinus rhythm was regained, and on 3 occasions atrial fibrillation resulted (one case returning spontaneously to sinus rhythm after 13 hours). Thus the conversion rate to sinus rhythm is 14%, and to atrial fibrillation 4%; the total conversion rate is 18%. On 8 occasions, conversion was achieved using a single extrastimulus (5 sinus rhythm, 3 atrial fibrillation). Four conversions used paired stimuli, and 2 used triple stimuli.

Table 6.1

ATRIAL FLUTTER - CLINICAL DATA

No.	Name	Age (yrs)	Male/ female M/F	Rate A (bpm)	Rate V (bpm)	Time in flutter (days)	Aetiology	Digoxin
1	NM	43	M	280	100	2	CCM	Yes
2	RP(1)	18	M	305	152	2	CHD	No
3	JI	58	M	250	125	2	SURG	Yes
4	JE	54	M	295	147	7	VHD	Yes
5	WL	61	M	300	136	14	IHD/BS	No
6	HM	66	F	310	155	14	HBP	No
7	RP(2)	19	M	220	110	1	CHD	No
8	WK	61	M	325	162	1	SURG	Yes
9	WW	68	M	280	140	2	I	Yes
10	LM	20	F	330	165	1	I	No
11	DS	61	M	280	140	3	AMI	Yes
12	AT	60	F	260	110	60	HBP	Yes
13	JR	73	M	350	120	6	I	Yes
14	JS(1)	53	F	330	105	>1year	SSS	No
15	JC	64	M	330	165	1	CCM	Yes
16	CM	55	F	245	123	1	VHD	No
17	TH	76	M	250	125	9	IHD	Yes
18	NG	71	M	260	130	7	IHD	Yes
19	MR	61	M	300	75	3	I	No
20	WW	69	M	255	85	>5years	IHD	Yes
21	JW	61	M	255	118	1	SURG	No
22	WC	70	M	350	120	1	IHD	No
23	HM	56	M	380	190	4	IHD/BS	No
24	MG	55	F	250	100	14	VHD	No
25	SS	55	M	270	135	15	HBP/DCM/Vasc	No
26	RU	69	M	280	140	5	I	Yes
27	EA	42	F	270	135	1	VHD	No
28	JG	47	M	305	76	60	IHD	Yes
29	CC	52	M	330	165	2	IHD/BS	No
30	RM(1)	39	M	280	140	2	VHD	No
31	NM(2)	45	M	230	115	2	CCM	No
32	AH	36	M	340	170	1	SURG	No
33	JB(1)	55	M	250	100	?	I	No
34	TA	46	M	300	150	?	COAD	No
35	RP	35	M	290	145	1	IHD/BS	No
36	LF	37	M	300	150	3	I	No
37	JR	49	M	300	150	1	IHD/BS	Yes
38	JS(2)	55	F	260	130	60	SSS	No
39	JB(2)	55	M	215	80	30	I	No
40	JI	73	M	320	80	3	AMI	Yes
41	RM(2)	40	M	300	150	4	VHD	No
42	FK	45	M	260	130	2	IHD/BS	No
43	RM(3)	40	M	300	150	2	VHD	No
44	RA	55	M	290	145	4	IHD	No

Table 6.1

ATRIAL FLUTTER - CLINICAL DATA

(continued)

No.	Name	Age (yrs)	Male/ female M/F	Rate A (bpm)	Rate V (bpm)	Time in flutter (days)	Aetiology	Digoxin
45	JT	74	M	300	150	7	I	No
46	JM	33	F	275	138	21	CHD	No
47	AF	69	M	280	140	12	IHD/BS	Yes
48	GK	53	M	300	100	5	IHD/BS	Yes
49	DC	60	M	230	115	14	IHD	No
50	MM	58	F	315	158	7	I	No
51	TN	62	M	300	150	1	IHD	No
52	JH	51	F	250	125	6 hours	IHD/SSS	No
53	JH(2)	51	F	320	160	10minutes	IHD/SSS	No
54	JM	56	M	285	95	1	IHD/BS	Yes
55	JV	50	M	255	85	2years	VHD	No
56	WM	52	M	320	160	3	IHD/BS	No
57	FM	40	M	300	150	6hours	I	No
58	EM	62	F	285	142	120	VHD	Yes
59	LK	20	F	215	108	>5years	CHD	No
60	GA	60	M	285	71	1	IHD	Yes
61	PB	79	M	280	112	2	I	No
62	HA	73	M	280	140	2	I	Yes
63	AS	43	F	250	125	42	VHD	Yes
64	TS	78	M	275	115	120	IHD	Yes
65	KO	38	M	325	162	1	IHD/BS	Yes
66	HM	50	F	255	128	10	I	No
67	AM	43	F	291	73	14	PPH	No
68	LA	59	M	263	132	1	MYOC	Yes
69	RG	60	M	265	132	14	VHD	Yes
70	DW	65	F	195	98	21	PPH	Yes
71	MC	50	M	280	120	60	VHD	No
72	MH	70	F	309	154	1	IHD	No
73	FD	69	M	264	132	7	VHD	No
74	RM(4)	42	M	293	146	7	VHD	No
75	EM	50	M	255	128	2	I	No
76	TS	50	M	292	146	2	I	No
77	WM	65	M	300	75	7	VHD	Yes
78	RQ	51	F	200	106	6000	VHD	Yes

Key to abbreviations :

A - atrium,
V - ventricle,
CCM - congestive cardiomyopathy,
CHD - congenital heart disease,
IHD - ischaemic heart disease,
BS - surgery involving cardiopulmonary bypass in the past month,
HBP - hypertension,
SURG - following non-cardiac surgery,
I - idiopathic,
AMI - acute myocardial infarction,
SSS - sick sinus syndrome,
DCM - dilated cardiomyopathy,
VHD - valvular heart disease
Vasc - Vasculitis
MYOC - myocarditis
PPH - primary pulmonary hypertension

Table 6.2

ATRIAL FLUTTER - ATRIOVERSION RESULTS

No.	Name	Atrial rate (bpm)	Digoxin	Window	Extrastimuli	Atrioversion
1	NM	280	Yes	1	no change	Sinus rhythm
2	RP(1)	305	No	1	no change	Sinus rhythm
3	JI	250	Yes	1	no change	AF(sustained)
4	JE	295	Yes	?	no change	AF(sustained)
5	WL	300	No	2	no change	Sinus rhythm
6	HM	310	No	1	no change	Sinus rhythm
7	RP(2)	220	No	1	no change	Sinus rhythm
8	WK	325	Yes	2	no change	Sinus rhythm
9	WW	280	Yes	?	no change	Sinus rhythm
10	LM	330	No	1	**Sinus rhythm (1 XST)**	
11	DS	280	Yes	2	no change	Sinus rhythm
12	AT	260	Yes	2	no change	AF-> SR
13	JR	350	Yes	2	no change	AF-> SR
14	JS(1)	330	No	2	no change	Sinus rhythm
15	JC	330	Yes	2	**AF-> SR (1 XST)**	
16	CM	245	No	2	no change	no change
17	TH	250	Yes	2	no change	AF(sustained)
18	NG	260	Yes	2	no change	AF(sustained)
19	MR	300	No	2	no change	AF(sustained)
20	WW	255	Yes	1	no change	AF(sustained)
21	JW	255	No	2	no change	AF-> SR
22	WC	350	No	2	no change	Sinus rhythm
23	HM	380	No	1	no change	Sinus rhythm
24	MG	250	No	2	no change	AF-> SR
25	SS	270	No	1	no change	Sinus rhythm
26	RU	280	Yes	2	no change	Sinus rhythm
27	EA	270	No	1	no change	AF(sustained)
28	JG	305	Yes	?	no change	AF-> SR
29	CC	330	No	2	no change	Sinus rhythm
30	AH	340	No	2	no change	no change
31	NM(2)	230	No	1	**Sinus rhythm (2 XST)**	
32	RM(1)	280	No	1	no change	Sinus rhythm
33	JB(1)	250	No	1	no change	Sinus rhythm
34	RP	290	No	1	no change	no change
35	TA	300	No	2	no change	Sinus rhythm
36	LF	300	No	1	no change	Sinus rhythm
37	JR	300	Yes	1	no change	no change
38	JS(2)	260	No	2	no change	no change
39	JB(2)	215	No	1	no change	Sinus rhythm
40	JI	320	Yes	1	**Sinus rhythm (3 XST)**	
41	RM(2)	300	No	1	no change	Sinus rhythm
42	FK	260	No	1	**Sinus rhythm (1 XST)**	
43	RM(3)	300	No	1	no change	Sinus rhythm
44	RA	290	No	1	no change	AF-> SR
45	JT	300	No	2	no change	AF(sustained)

Table 6.2

ATRIAL FLUTTER - ATRIOVERSION RESULTS

(continued)

No.	Name	Atrial rate (bpm)	Digoxin	Window	Extrastimuli	Atrioversion
46	JM	275	No	1	**Sinus rhythm (2 XST)**	
47	AF	280	Yes	1	no change	Sinus rhythm
48	GK	300	Yes	1	no change	Sinus rhythm
49	DC	230	No	1	no change	Sinus rhythm
50	MM	315	No	1	no change	Sinus rhythm
51	TN	300	No	1	no change	Sinus rhythm
52	JH	250	No	1	**Sinus rhythm (1 XST)**	
53	JH(2)	320	No	1	no change	Sinus rhythm
54	JM	280	Yes	1	no change	Sinus rhythm
55	JV	255	No	1	no change	AF(sustained)
56	WM	320	No	1	no change	AF(-> SR)
57	FM	300	No	1	no change	AF(-> SR)
58	EM	285	Yes	2	no change	no change
59	LK	215	No	1	**Sinus rhythm (2 XST)**	
60	GA	285	Yes	1	no change	AF(-> SR)
61	PB	280	No	1	no change	AF
62	HA	280	Yes	1	no change	AF(sustained)
63	AS	250	Yes	1	no change	Sinus rhythm
64	TS	275	Yes	1	**Sinus rhythm (1 XST)**	
65	KO	325	Yes	1	**Sinus rhythm (3 XST)**	
66	HM	255	No	2	**AF (1 XST)**	
67	AM	291	No	1	no change	Sinus rhythm
68	LA	263	Yes	2	no change	AF (sust)
69	RG	265	Yes	2	**Sinus rhythm (1 XST)**	
70	DW	195	Yes	1	no change	Sinus rhythm
71	MC	280	No	1	no change	AF (sust)
72	MH	309	No	2	no change	no change
73	FD	264	No	2	**AF (1 XST)**	
74	RM(4)	293	No	1	no change	no change
75	EM	255	No	1	no change	Sinus rhythm
76	TS	292	No	1	no change	Sinus rhythm
77	WM	300	Yes	2	no change	AF (sust)
78	RQ	200	Yes	1	**SR (2 XST)**	

Key to abbreviations :

AF - atrial fibrillation,
XST - extrastimulus,
-> SR - spontaneously returning to sinus rhythm in less than 48 hours

Table 6.3

ATRIAL FLUTTER - CONVERSION USING EXTRASTIMULI

	Single stimulus	One or two stimuli	One, two or three stimuli
No. of cases	78	78	78
Sinus rhythm	5	9	11
Atrial fibrillation (-> SR < 48 hrs)	1	1	1
Atrial fibrillation (sustained)	2	2	2
No change	70	66	64
Total conversion rate*	10.3%	15.4%	18.0%
Immediate conversion to SR	6.4%	11.5%	14.1%
Immediate conversion to AF	3.8%	3.8%	3.8%
Spontaneous return to SR**	33%	33%	33%
Total conversion to SR	7.6%	12.8%	15.4%

Key:
SR - sinus rhythm
AF - atrial fibrillation
sustained - AF sustained or requiring cardioversion

(Note:
* "Total conversion rate" is the % of cases in whom flutter was converted either to SR or AF.
** "Spontaneous return to SR" means the % of those cases converted to AF who return to SR in less than 48 hours.)

Ten of the 11 conversions to sinus rhythm occurred at Type I sites, whereas all of the 3 conversions to atrial fibrillation occurred at Type II sites (significant; $p<0.05$ using the Fourfold Table Test). Thus, although incidence of rhythm conversion was the same for Type I and Type II windows, conversion was more likely to result in sinus rhythm at a Type I site.

The overall low success rate (18%) compares very unfavourably with the 86.5% achieved using rapid atrial pacing (see Table 2.1), and confirms that combinations of conventional extrastimuli are seldom useful in conversion of atrial flutter.

6.3 Results using Atrioversion

6.3.1 Overall results

In the remaining 64 cases, Atrioversion was attempted. Conversion of rhythm was achieved in 56 cases (88%). Thirty-three cases (52%) were converted to sinus rhythm, and 23 (36%) to atrial fibrillation. In 8 cases (12%), atrial flutter persisted.

Of the 23 conversions to atrial fibrillation, 9 spontaneously returned to sinus rhythm within 48 hours, while 14 remained in atrial fibrillation or were electively cardioverted. Thus, eventual conversion to sinus rhythm was achieved in 42 cases (66%). These figures are summarised in Table 6.4, together with comparative figures using rapid atrial pacing (from Table 2.1).

When the use of extrastimuli is included, there were 44 immediate conversions to sinus rhythm in 78 cases (56%), and a further 10 cases spontaneously regained sinus rhythm, giving an overall conversion to sinus rhythm of 69%.

6.3.2 Comparison with rapid atrial pacing

Table 6.3 shows that one, two or three extrastimuli with 2 ms pulse width are effective in only 18% of cases. Most other workers confirm these findings (see Chapter 2). However, Table 6.4 shows that results obtained using single, long

Table 6.4

ATRIAL FLUTTER

CONVERSION USING ATRIOVERSION vs RAPID ATRIAL PACING

	ATRIOVERSION	RAPID ATRIAL PACING (pooled data)
No. of cases	64	505
Sinus rhythm	33	249
Atrial fibrillation (-> SR <48 hours)	9	101
Atrial fibrillation (sustained)	14	89
No change	8	66

(Chi-squared = 0.12 - not significant)

Total conversion rate	87.5%	86.9%
Immediate conversion to SR	51.6%	49.3%
Immediate conversion to AF	35.9%	37.6%
Spontaneous return to SR	39.1%	53.2%
Total conversion to SR	65.6%	69.3%

Key:

SR	- sinus rhythm
AF	- atrial fibrillation
sustained	- AF sustained or requiring cardioversion

constant current pulses to convert atrial flutter are very similar to those obtained using rapid atrial pacing. A chi-squared test showed no significant difference between the results of Atrioversion and the pooled data using rapid atrial pacing (chi-squared = 0.12, 3 degrees of freedom).

6.3.3 Effect of duration of flutter

It was shown in Chapter 2 that the duration of atrial flutter had an important bearing on the chances of successful conversion using rapid atrial pacing; in patients with duration less than 24 hours, conversion rate to sinus rhythm was significantly higher. Since all but 3 of the cases in the Atrioversion series had a duration of at least 24 hours, these cases should be compared to the subset of similar patients using rapid atrial pacing (see Table 2.3). This comparison is made in Table 6.5. Again, it can be seen that all conversion rates are very similar to those found using rapid pacing. In summary, therefore, overall results would suggest that Atrioversion has the same success rate as rapid atrial pacing in converting atrial flutter - conversion of rhythm in 90% of cases, and direct conversion to sinus rhythm in 50%.

6.3.4 Factors influencing successful conversion

It may be possible to identify factors which influence the success rate in the Atrioversion series.

The cases were subdivided into groups on the basis of outcome (using conversion to sinus or AF as the discriminant function). Stepwise regression was then performed on the groups to identify factors predicting conversion to either sinus rhythm or to AF.

The following parameters were included as predictors for each case.

1) sex

2) atrial rate

3) Duration of flutter

Table 6.5

ATRIAL FLUTTER

CONVERSION USING ATRIOVERSION vs RAPID ATRIAL PACING

[Patients with flutter duration of at least 24 hours]

	ATRIOVERSION	RAPID ATRIAL PACING (pooled data)
No. of cases	62	143
Sinus rhythm	32	68
Atrial fibrillation (-> SR <48 hours)	8	27
Atrial fibrillation (sustained)	14	32
No change	8	16

(Chi-squared = 0.10 - not significant)

Total conversion rate	87.1%	88.8%
Immediate conversion to SR	51.6%	47.6%
Immediate conversion to AF	35.5%	41.3
Spontaneous return to SR	36.4%	45.8%
Total conversion to SR	64.5%	66.5%

Key:

SR	- sinus rhythm
AF	- atrial fibrillation
sustained	- AF sustained or requiring cardioversion

4) ischaemic heart disease

5) valvular heart disease

6) digoxin

7) type of window

Variables (1) to (3) are continuous, and variables (4) to (7) are discretised binary variables (e.g. digoxin= 1 or 0 depending if the patient is or is not digitalised).

Analysis was performed using a proprietary statistical package (Minitab) running on a Prime computer.

The following variables were **not** included in the analysis after it was shown that they were not independent of one or more of the variables listed above.

- age (positively correlated with digoxin, see above)
- 2:1 AV block (negatively correlated with age and atrial rate)

Stepwise regression analysis was performed, and variables were sequentially rejected from the model on the basis of having the lowest F-statistic calculated from a model including all remaining variables. The process is repeated with the reduced variable set until no further parameters can be rejected. The rejection criterion is that the calculated F-statistic is less than a minimum value of the F-ratio; the default value of F-ratio=4 was used. An overall correlation coefficient is eventually obtained, with individual regression coefficients for each predictor remaining in the model.

6.3.5 Results of stepwise regression analysis

Using either conversion to sinus or conversion to AF as discriminant parameters, only one variable was a significant predictor: type of excitable window. All other variables were rejected from the model. A Type I window was more likely to result in conversion to sinus rhythm ($r=0.38$, $p<0.001$). Similarly, a Type I response was less likely to result in conversion to AF ($r=-0.35$, $p<0.002$).

6.3.6 Excitable window

A Type I excitable window was defined in Chapter 4 as a stimulation site where the return cycle following an atrial extrastimulus was not compensatory, and minimally exceeded the basic atrial flutter cycle length. A Type II window demonstrated longer, or fully compensatory, pauses. The significance of these types of response is seen in Table 6.6. In 48 patients who exhibited a Type I response, 34 (71%) were converted to sinus rhythm using extrastimuli or Atrioversion, whereas only 9 out of 27 (33%) of Type II responses were converted to sinus rhythm. A chi-squared analysis showed that this difference was significant (chi-squared=9.93, $p < 0.005$).

When Atrioversion alone is considered, conversion to sinus rhythm is again significantly higher in Type I cases (63%) than in Type II (35%) (chi-squared=4.63, $p < 0.05$)

6.3.7 Optimising successful conversion rate

The important factor affecting successful conversion, namely the type of excitable window found, is readily alterable. In the present study, it was usually possible to find a Type I window if a careful search of the right atrial endocardium is made. Hence, it is possible to maximise the success of Atrioversion by carefully searching for a suitable stimulation site. If a Type I response is found, the conversion rate to sinus rhythm is higher than for rapid atrial pacing (chi-squared=8.13, $p<0.005$; see Table 6.7).

Table 6.6

ATRIAL FLUTTER - EXTRASTIMULI + ATRIOVERSION

Conversion rate - effect of type of excitable window

	TYPE I WINDOW	TYPE II WINDOW
No. of cases	48	27
Sinus rhythm	34	9
Atrial fibrillation	11	13
No change	3	5

(chi-squared = 9.93, $p < 0.005$)

When a Type I response was found, conversion to sinus rhythm was more likely (see text for multivariate analysis).

Table 6.7

CONVERSION OF ATRIAL FLUTTER

ATRIOVERSION SERIES vs RAPID ATRIAL PACING (pooled data)

Atrioversion cases with Type I excitable window

	ATRIOVERSION SERIES	RAPID ATRIAL PACING (pooled data)
No. of cases	48	505
Sinus rhythm	34	249
Atrial fibrillation	11	190
No change	3	66

(Chi- squared = 8.13, $p < 0.005$)

Conversion to sinus rhythm was more likely in the Atrioversion series.

6.4 Individual cases

6.4.1 Conversions using conventional extrastimuli

Figures 6.6 to 6.11 show 6 of the 12 conversions which were achieved using conventional extrastimuli.

Case 42

Following multiple vein grafting, a 45 year old man with coronary artery triple vessel disease developed atrial flutter (Figure 6.6). Despite the modest ventricular rate (130 bpm), he rapidly went into left ventricular failure, and was considered unsuitable for cardioversion. Atrial flutter cycle length was 220 ms, and was terminated with a single extrastimulus, delivered to the low lateral right atrium, at a coupling time of 155 ms. A single, flutter-like, atrial beat follows the extrastimulus, followed by termination, and return to sinus rhythm.

Case 52

Figure 6.7 again shows termination of flutter (cycle length 240 ms) by a single extrastimulus, coupled at 130 ms. Once again, there is a single atrial beat following the extrastimulus. This beat is followed by a long pause before a sinus P-wave ensues; during this pause, there is a single ventricular beat from a permanent pacemaker (implanted on the same day for control of bradycardia-tachycardia syndrome). After the pause and sinus escape beat, atrial flutter immediately restarts.

Case 31

In Figure 6.8, the flutter cycle length is 212 ms. Two high right atrial stimuli (both coupled at 150ms) cause conversion to sinus rhythm. There are two points of interest here - firstly, the two extrastimuli are again followed by a single,

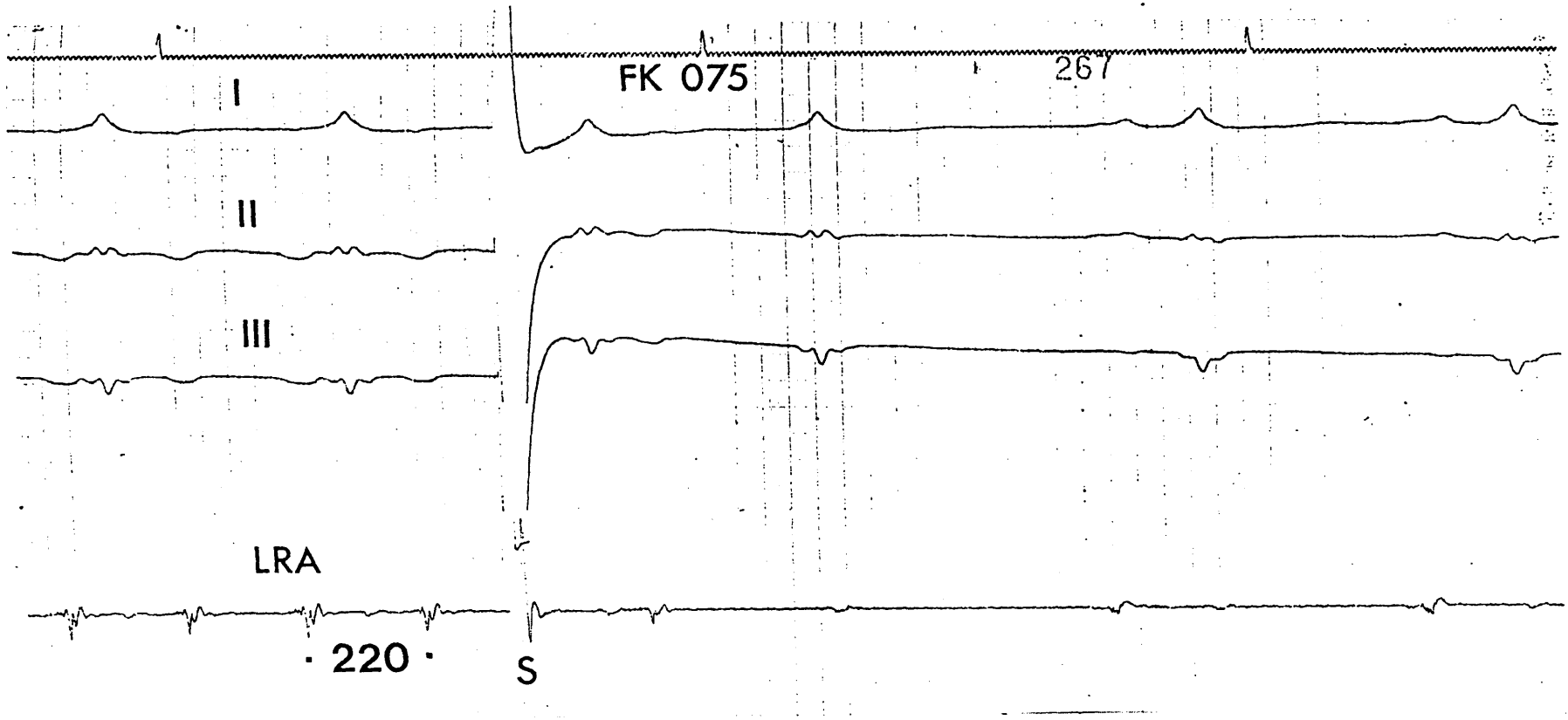


Figure 6.6

Case 42. Atrial flutter, cycle length 220 ms, is converted to sinus rhythm by a single extrastimulus, delivered to the low lateral right atrium. A single flutter-like beat follows the stimulated beat and precedes conversion.

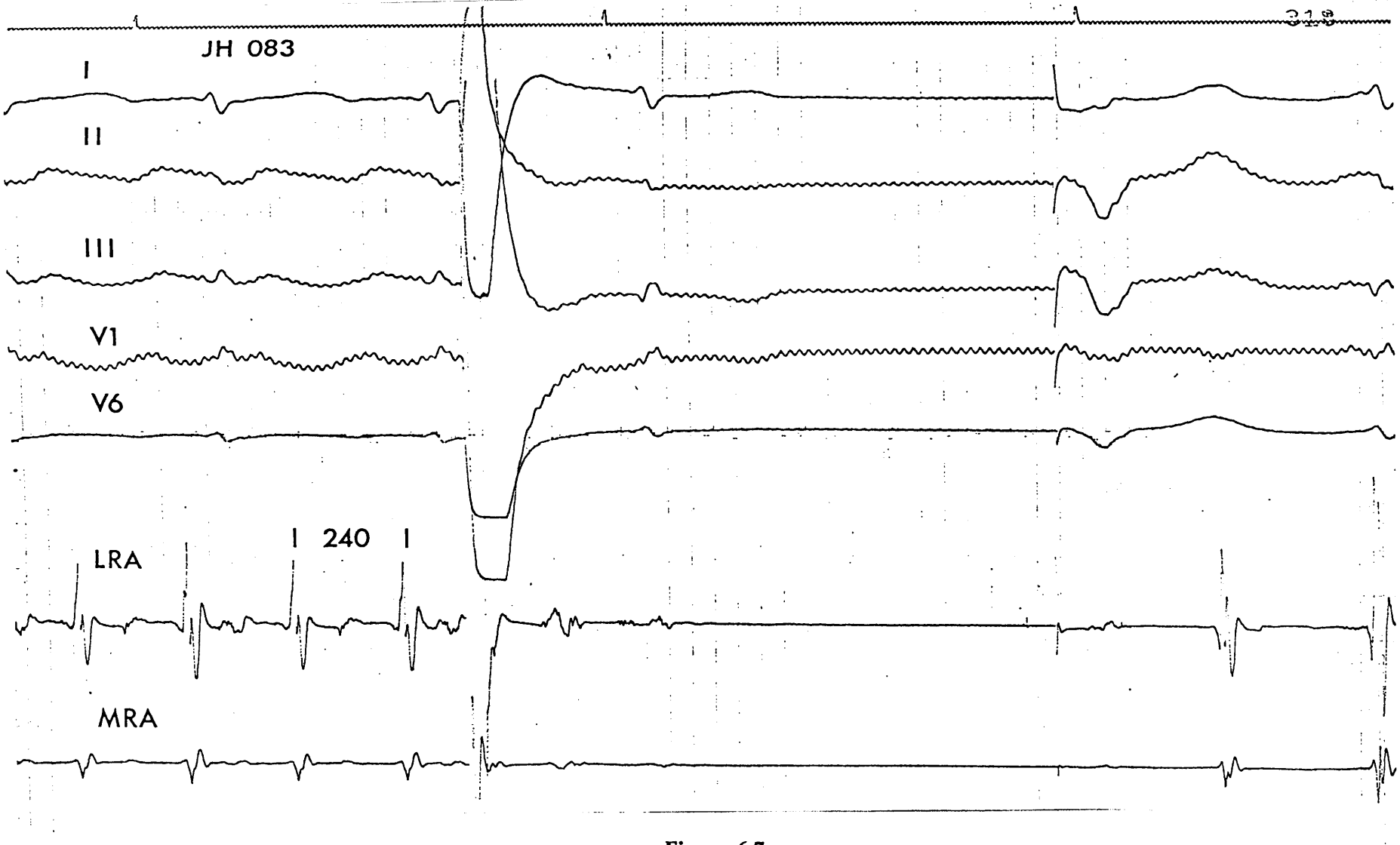


Figure 6.7

A single extra stimulus terminates flutter in case 52. The premature beat in the low lateral right atrium is again followed by a single flutter-like beat, then by a long pause (during which a permanent pacemaker delivers a stimulus) before sinus rhythm resumes.

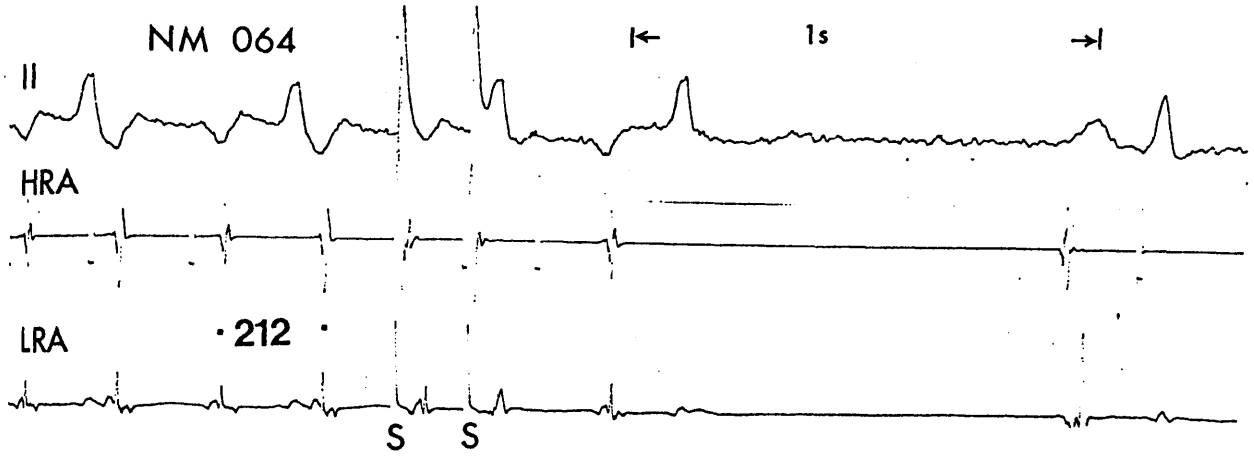


Figure 6.8

Case 31. Paired high right atrial stimuli terminate flutter. A single atrial escape beat precedes conversion.

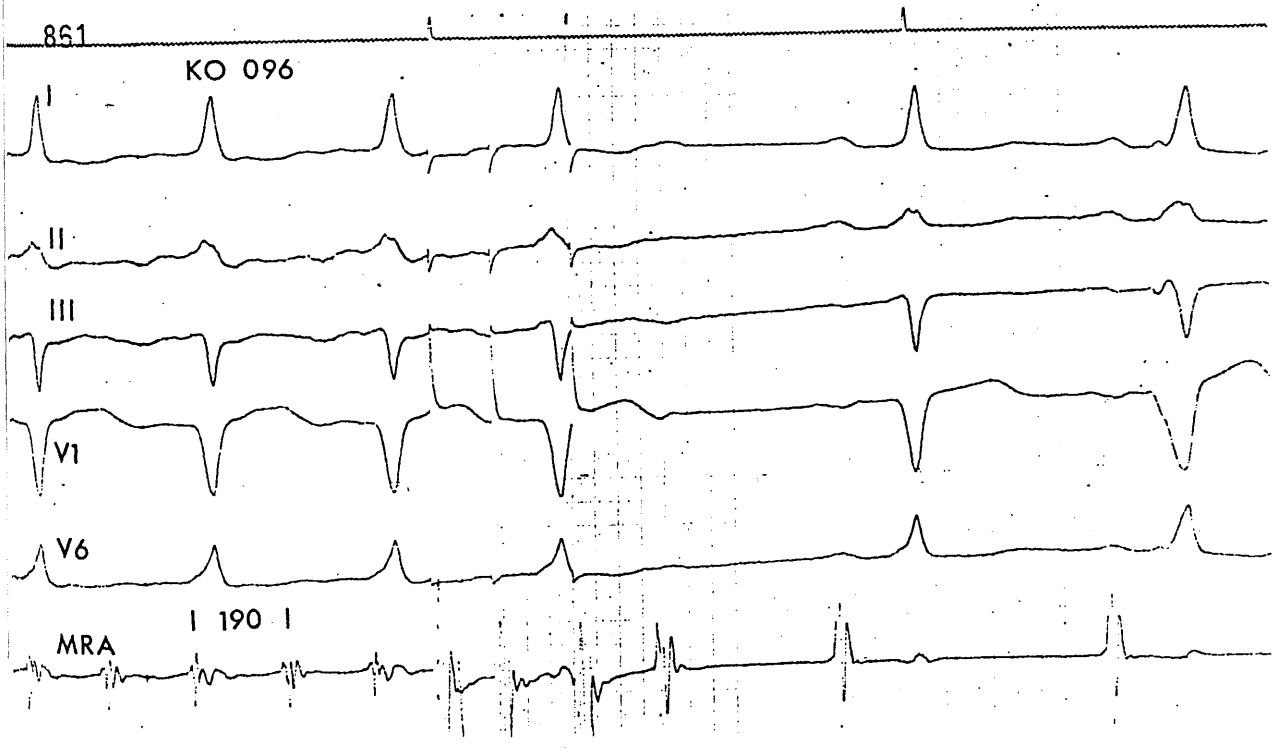


Figure 6.9

A rapid atrial flutter (cycle length 190 ms) in case 65 is converted with three stimuli to the mid right atrium. The single escape beat is again present.

flutter-like beat preceding termination; and secondly, the first stimulus, although capturing the high right atrium, does not affect the low right atrial trace, and only when the second stimulus is added does the low right atrial trace show a change. This is a demonstration of "peeling-back" of refractoriness (Josephson, 1979), where the first stimulus, although not capturing the low atrial site, alters the refractoriness of the intervening tissue sites, and allows the second stimulus to capture the distant site.

Case 65

In Figure 6.9, a rapid flutter is seen (atrial cycle length 190 ms). Flutter is converted by three extrastimuli delivered to the mid-lateral right atrium (coupling times 120, 130 and 170 ms). Once again, a flutter-like beat follows the extrastimuli. The very rapid resumption of the sinus mechanism implies that some degree of atrio-sinus block was present during flutter, but that the sinus node automaticity was not depressed.

Case 59

This case is shown in Figure 6.10. This 19 year old girl had a surgically corrected atrial septal defect, and had been in atrial flutter, controlled by propranolol, since a failed attempt at conversion in 1979, using cardioversion, had briefly produced atrial fibrillation, quickly reverting to flutter. She had thus been in atrial flutter for at least 5 years prior to Atrioversion. Her atrial rate had slowed over these 5 years, from 280 bpm to 215 bpm, with a constant 2:1 ventricular response. Paired stimuli delivered to the mid-lateral right atrium resulted in six beats of an accelerated rhythm, followed by atrial asystole for 3.4 seconds, before the long-dormant sinus node began to function. This patient was still in sinus rhythm at follow-up, 3 months later.

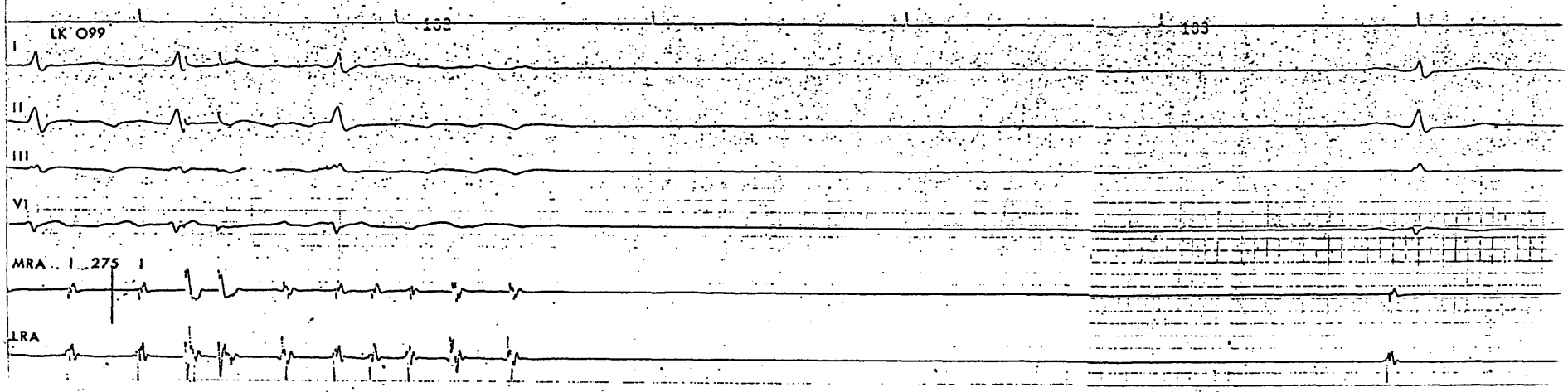


Figure 6.10

Case 59. Atrial flutter of over 5 years duration. Two right atrial stimuli induce a short burst of flutter-fibrillation, followed after a 3 second pause by sinus rhythm.

Case 15

Figure 6.11 shows a conversion to atrial fibrillation with a single stimulus. The flutter cycle length is 180 ms, and the stimulus is coupled at 110 ms. This man returned spontaneously to sinus rhythm 24 hours later.

In the remaining 5 conversions to sinus rhythm using extrastimuli, there was a brief period of atrial fibrillation or accelerated flutter preceding sinus rhythm. In cases 10 and 40, there were respectively 3 and 6 beats of an irregular rapid atrial rhythm which preceded sinus rhythm. Cases 46 and 64 were converted to an accelerated atrial flutter, which terminated after 9 and 36 seconds, respectively.

Although Disertori (1983) achieved conversion in 10 of 13 patients, direct conversion occurred in only 3. In the remaining 7, a period of atrial fibrillation or faster flutter preceded sinus rhythm. It is interesting that all three of Disertori's direct conversions used triple extrastimuli, and in all three cases, conversion was preceded by a "*final, spontaneous, flutter-like atrial beat*", just as is seen in the four Figures above. Similarly, the study of Gloor (1986) showed 3 examples of conversion using 1, 2 and 3 extrastimuli, and conversion was preceded by respectively 3, 2 and 1 repetitive atrial beats. These final repetitive beats appears to be characteristic of the conversion response of atrial flutter to extrastimuli.

In summary, there are two clear mechanisms of conversion of atrial flutter to sinus rhythm using extrastimuli:

1) Conversion via an intervening spell of atrial fibrillation or accelerated flutter, reverting spontaneously to sinus (6 cases)

2) Sinus rhythm immediately follows the stimuli, with only one intervening, flutter-like atrial beat (5 cases).

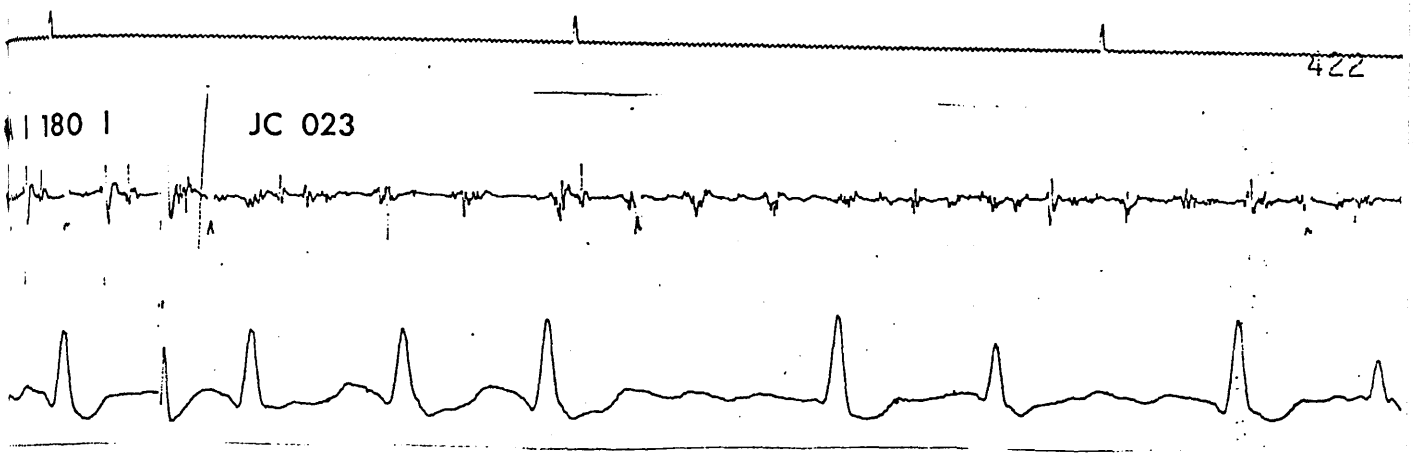


Figure 6.11

Case 15. A single stimulus induces atrial fibrillation. Flutter cycle length is 180 ms. Note the double atrial deflections recorded from the mid right atrium. These split electrograms are probably due either to slow local conduction or to an area of block, with remote recording from two dissociated areas.

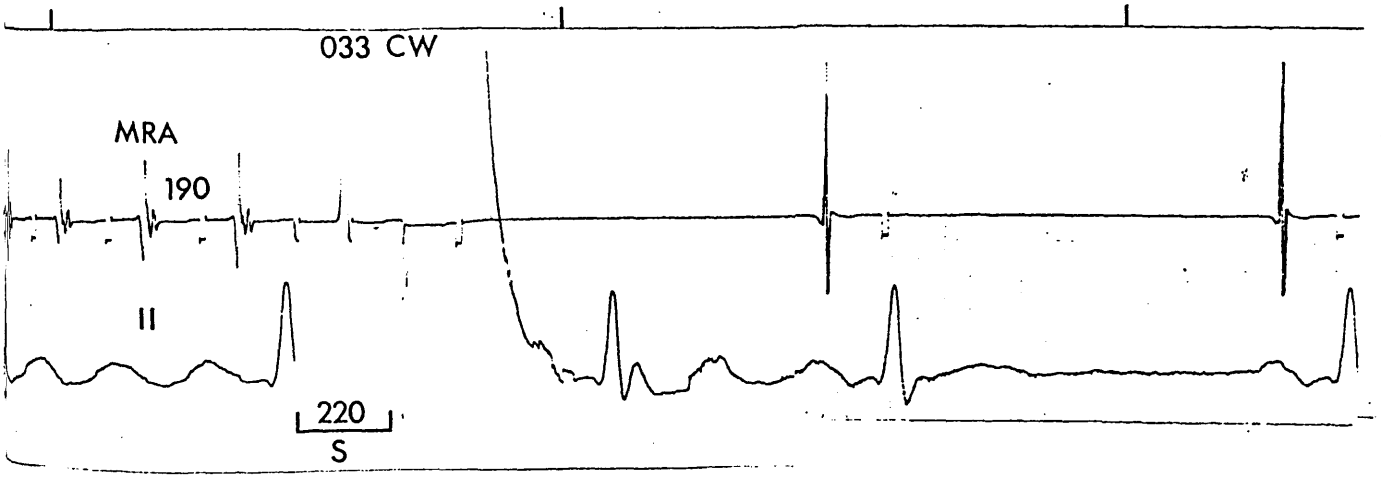


Figure 6.12

Case 22. Atrial flutter (cycle length 190 ms) is converted to sinus rhythm by a long pulse (duration 220 ms) delivered to the mid lateral right atrium. There is local atrial asystole, followed by resumption of sinus rhythm.

This study has demonstrated that, in a small proportion (approximately 13%) of cases, it is possible to convert atrial flutter to sinus rhythm using conventional extrastimuli, without an intervening period of atrial fibrillation. Such conversion using single and paired stimuli (Figures 6.6, 6.7 and 6.8) has been previously demonstrated only once (Gloor, 1986).

6.4.2 Atrioversion - conversions to sinus rhythm

Figures 6.12, 6.13, 6.14 and 6.15 show conversions to sinus rhythm, following an Atrioversion stimulus.

Case 22

In Figure 6.12 the flutter cycle length is 190 ms. An impulse delivered to the mid-lateral right atrium, with a coupling time of 105 ms, and pulse width 220 ms, appears to cause local atrial asystole, followed by sinus rhythm after 1.3 seconds. Surface lead II displays a large offset after the stimulus, and it is difficult to estimate whether there may be any atrial activity present.

Cases 33, 48 and 54

The next three Figures, 6.13, 6.14 and 6.15, show very typical conversions. In all cases, the long Atrioversion stimulus is followed by several accelerated, irregular atrial beats, lasting in each case for around 1 second, and followed by atrial asystole, which allows sinus rhythm to resume.

Case 43

Figure 6.16 gives an interesting insight into the mechanism of conversion. This patient had previously undergone aortic valve replacement, and had developed atrial flutter on two previous occasions, on which he was successfully Atrioverted (cases 32 and 41). Five surface leads and three simultaneous

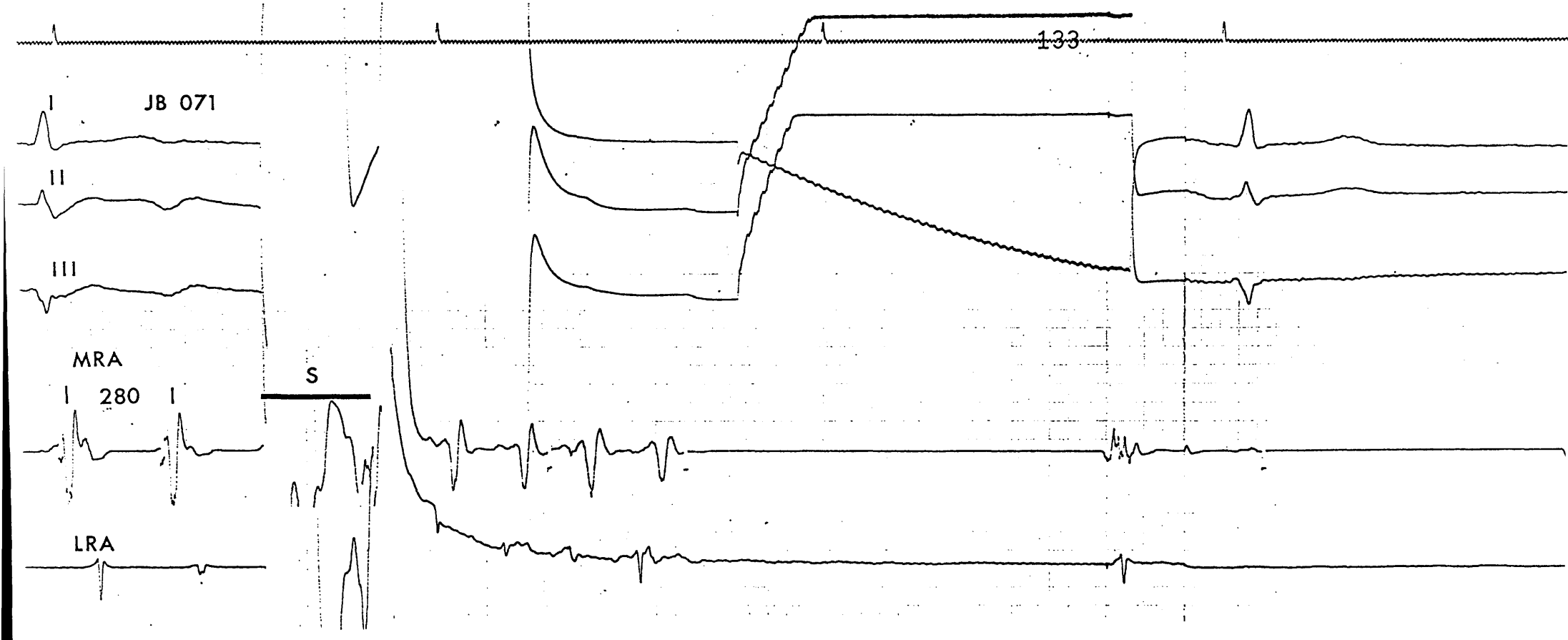


Figure 6.13

Case 39. A typical pattern of Atrioversion to sinus rhythm. A long stimulus to the mid right atrium is followed by 4 irregular atrial beats, and then resumption of sinus rhythm.

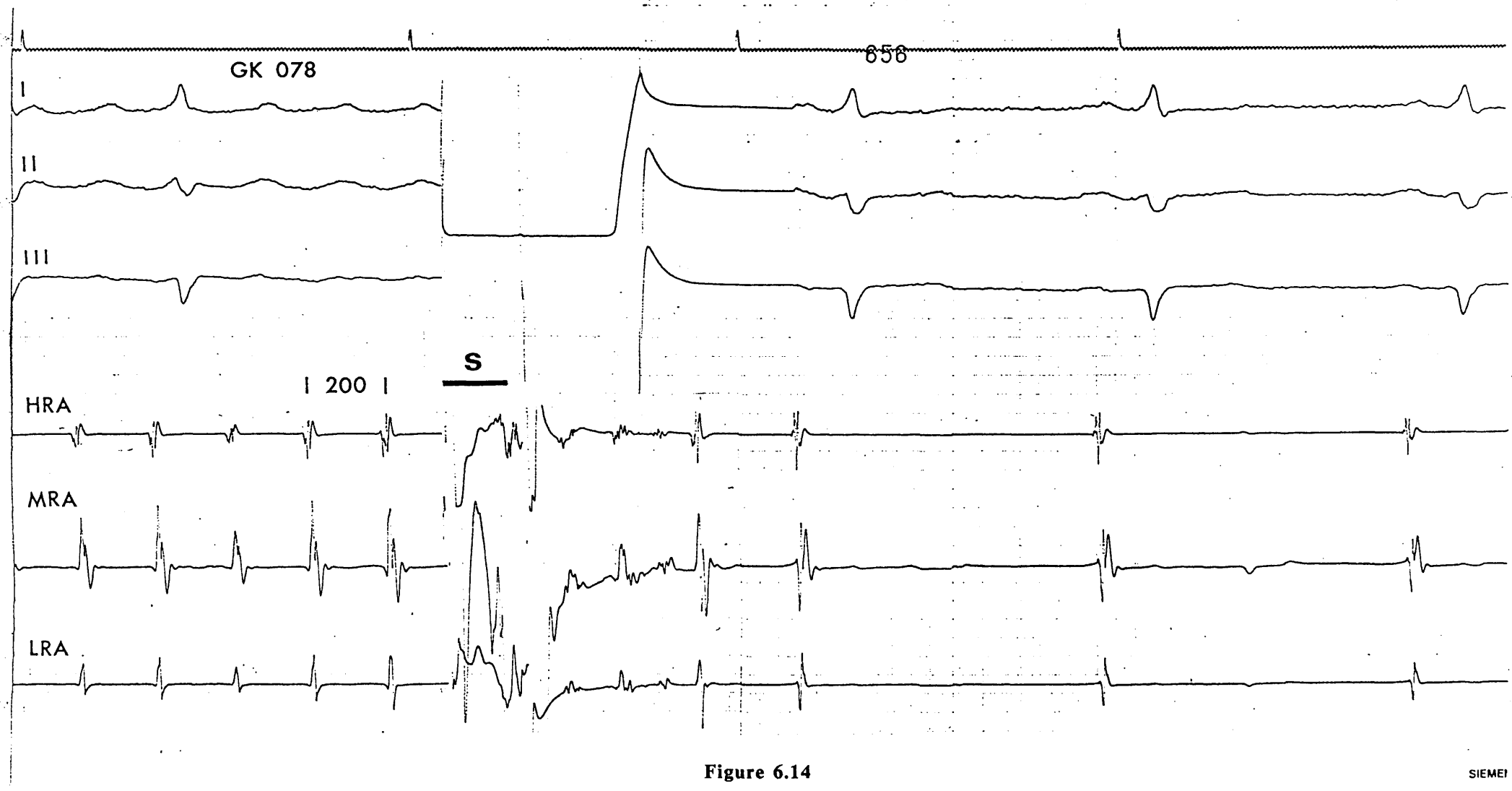


Figure 6.14

Case 48. As in Figure 6.13, Atrioversion is followed by several irregular atrial beats before sinus rhythm resumes. The first sinus impulse is preceded by only a short pause, suggesting that the sinus node was "protected" from the prior rapid atrial rate by some degree of atrio-sinus block.

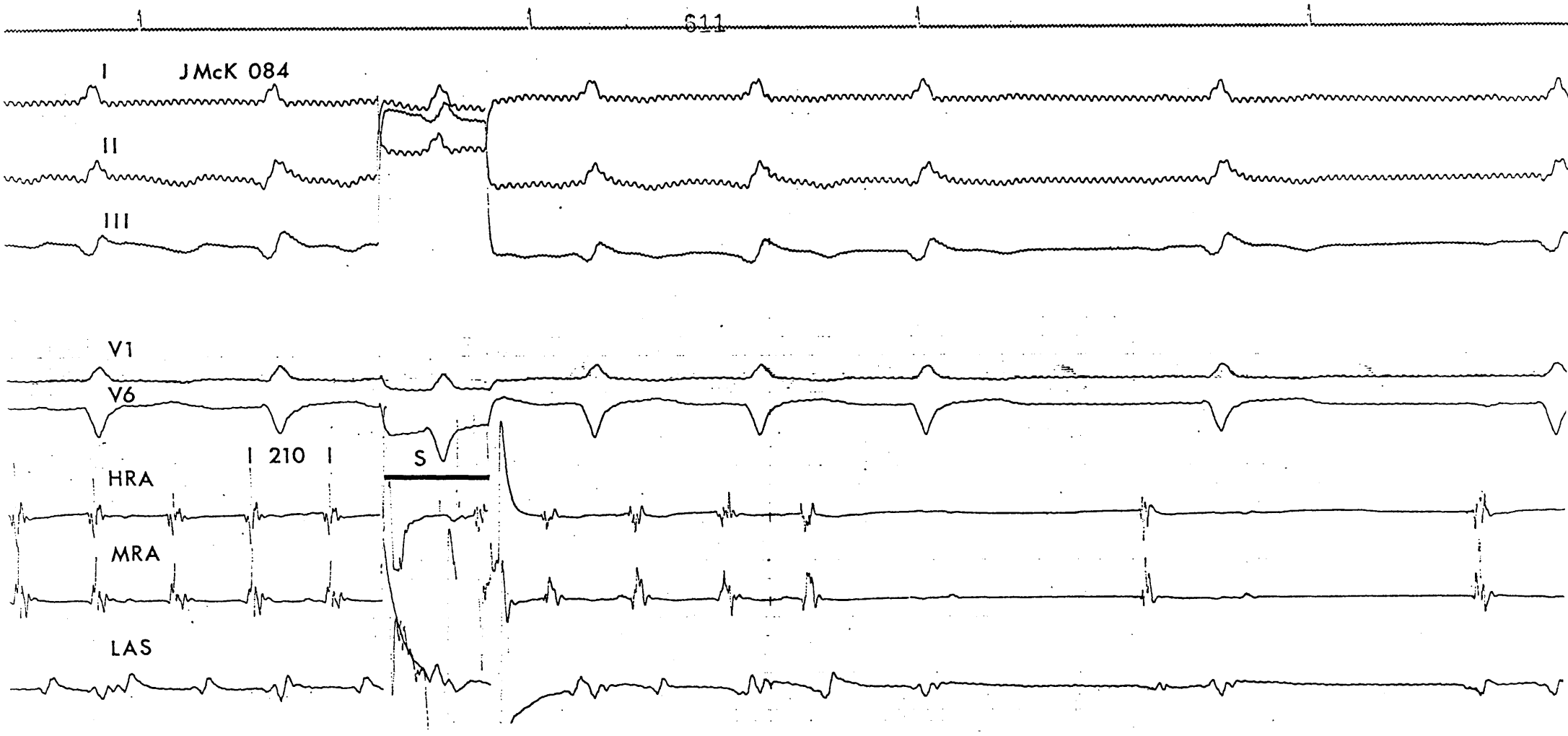


Figure 6.15

Case 54. Atrioversion is again followed by irregular atrial beating for 1 second before sinus rhythm resumes. In this and the previous two figures, the long impulse is delivered at a delay of 65-75% of the flutter cycle length, and a pulse width 10-20% longer than the flutter cycle length.

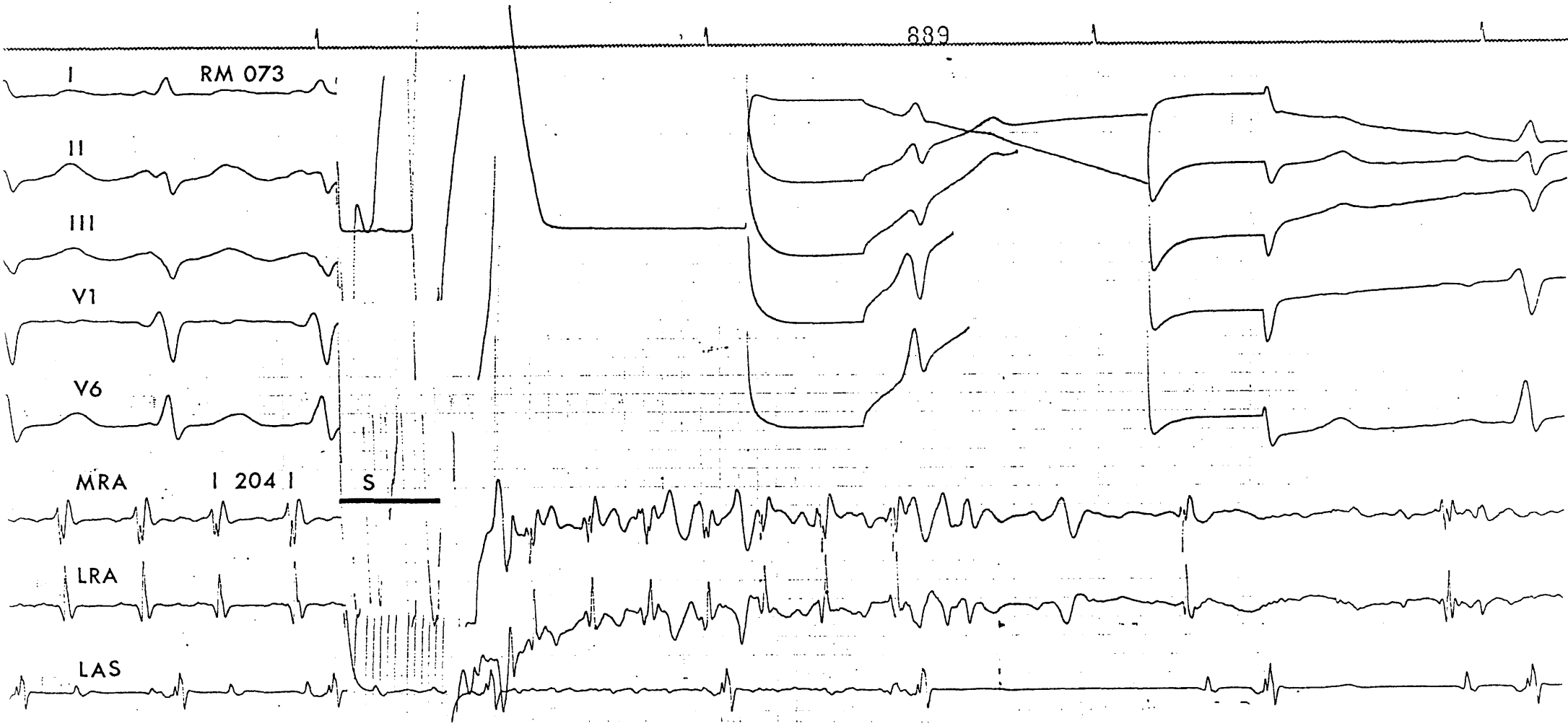


Figure 6.16

Case 43. Atrial flutter of cycle length 204 ms is seen. A 250 ms duration impulse to the mid lateral right atrium induces fibrillation in the low septal trace (LAS) and an accelerated atrial rhythm in the lateral wall. After 2 seconds, atrial asystole occurs, followed by sinus rhythm.

bipolar atrial traces are shown. The three intraatrial electrograms were recorded from the mid and low lateral right atrium, and from the low interatrial septum. Following a stimulus to the mid right atrium, the lateral wall traces show a regular, accelerated atrial rhythm, terminating spontaneously after less than 2 seconds; however, the low septal trace shows local atrial fibrillation, which appears to terminate into asystole just before the other two intra-atrial traces. This is a demonstration of transient co-existing flutter and fibrillation.

Conversion preceded by brief repetitive activity occurred in 28 cases, with the accelerated rhythm lasting for between 1 beat and 10 seconds. In 5 cases, there was a short run of pure atrial fibrillation, with no recognisable organised atrial rhythm in any surface or intracardiac traces, and of less than 15 seconds duration, before sinus rhythm.

The traces demonstrate that it is generally not possible to produce atrial asystole using Atrioversion, and that conversion of rhythm is generally preceded by a short period of accelerated or irregular beating. This conclusion is not entirely surprising, bearing in mind that, even if a focus or small circuit is extinguished by the impulse, the distant parts of the atria may be thrown out of their equilibrium by the extinction of the central focus or circuit, and these parts may give rise to a fibrillation-like rhythm, which may or may not be sustained. Further examination of the mechanism of conversion is needed, with many more electrograms being recorded from distant atrial sites - an experiment which would probably have to be carried out in vitro.

6.4.3 Atrioversion - Conversions to atrial fibrillation

Figures 6.17 to 6.21 show five Atrioversions to atrial fibrillation.

Case 45

In Figure 6.17 the flutter cycle length is 200 ms. A stimulus is applied to the right atrial appendage, at 155 ms coupling time, and immediate conversion to atrial fibrillation occurs. The regular atrial contractions on the surface ECG disappear, although the intra-atrial trace shows coarse fibrillation waves with an approximate rate of 500 per minute. This rhythm was sustained, and the patient was eventually digitalised.

Cases 61 and 62

In the next two Figures (6.18 and 6.19), surface lead I has been replaced by a right atrial pressure trace. In Figure 6.18, atrial flutter is seen, with cycle length 215 ms. Intracardiac electrograms are from the mid atrial septum, and the mid and high lateral right atrial wall. A stimulus to the septal site, at coupling time 145 ms, results in fibrillation. Coarse atrial waves are seen in leads II and V1 after conversion, but there is no regular organised atrial activity, as can be seen by the lack of atrial pressure waves. It is interesting to note that, during the long impulse, the high right atrium continues to beat, but at a much reduced cycle length. The mid lateral wall shows no depolarisations during the impulse, but returns to its 1:1 relationship with the high right atrium after the stimulus. The septal trace initially maintains 1:1 conduction with the lateral wall, but after 1 second, it becomes fractionated, and loses its regularity. It would appear that the Atrioverting impulse converted flutter to fibrillation, which quickly reverted to sinus rhythm. It is also feasible, although less likely, that the impulse suppressed the original cause of flutter, whether focus or circuit, but that smaller wavelets continued afterwards, which were too rapid for both atria to maintain. Figure 6.19 (case 62) shows a very similar pattern. The impulse is delivered to the mid right atrium, and fibrillation results. The low right atrial trace shows accelerated flutter-fibrillation afterwards, and block develops between low and mid atrial sites.

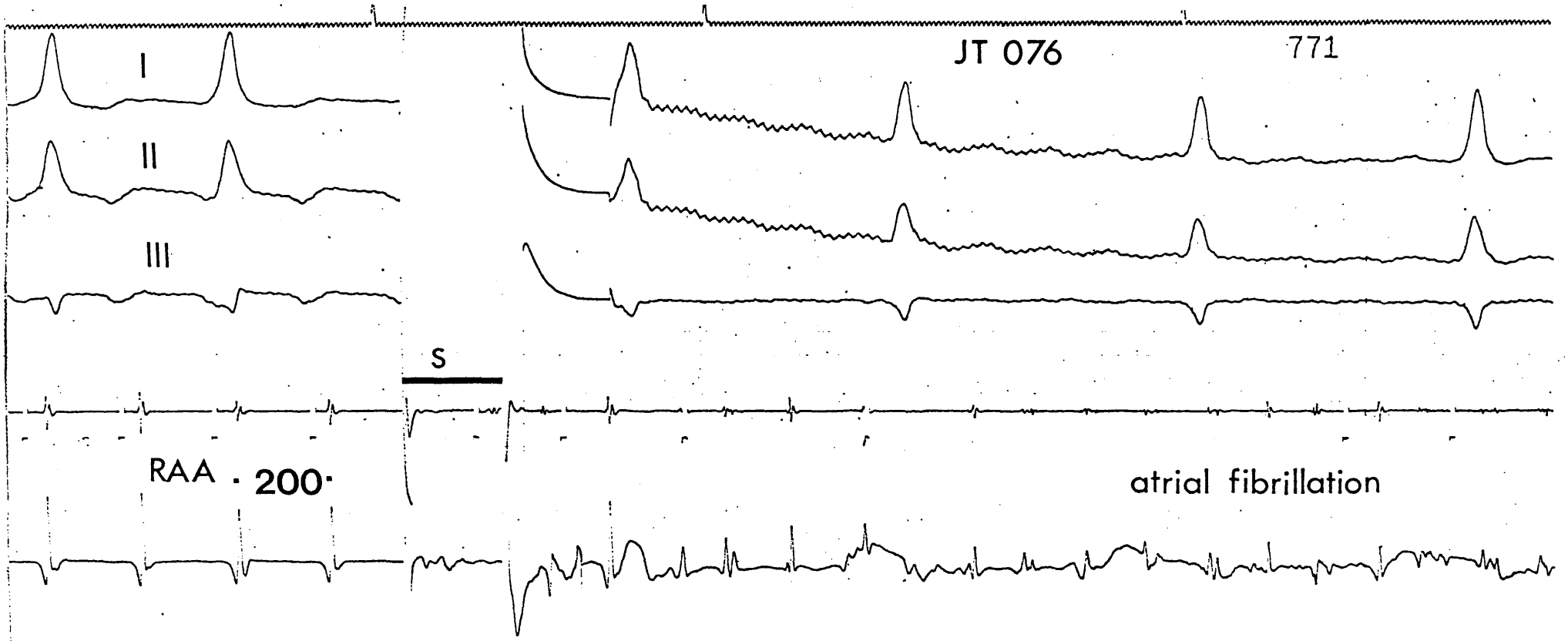


Figure 6.17

Case 45. Induction of atrial fibrillation by a long stimulus. The fibrillation is initially coarse, with quasi-regular atrial electrograms in the right atrial appendage.

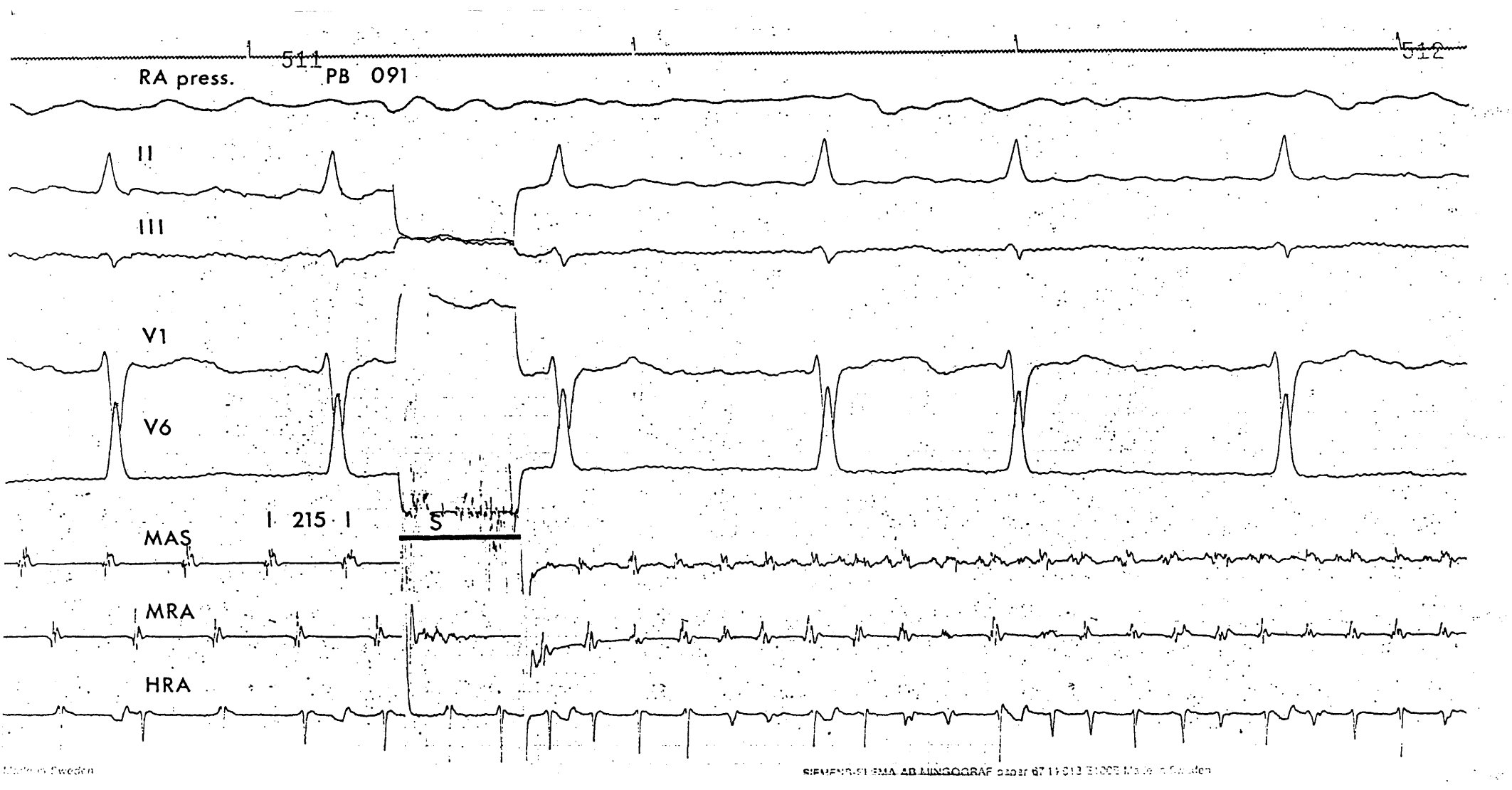


Figure 6.18

Case 61. Right atrial pressure trace, four surface ECG leads and three intracardiac electrograms show conversion of atrial flutter to atrial fibrillation by a long stimulus. Initial coarse fibrillation waves are not associated with atrial contraction, as seen from the pressure trace.

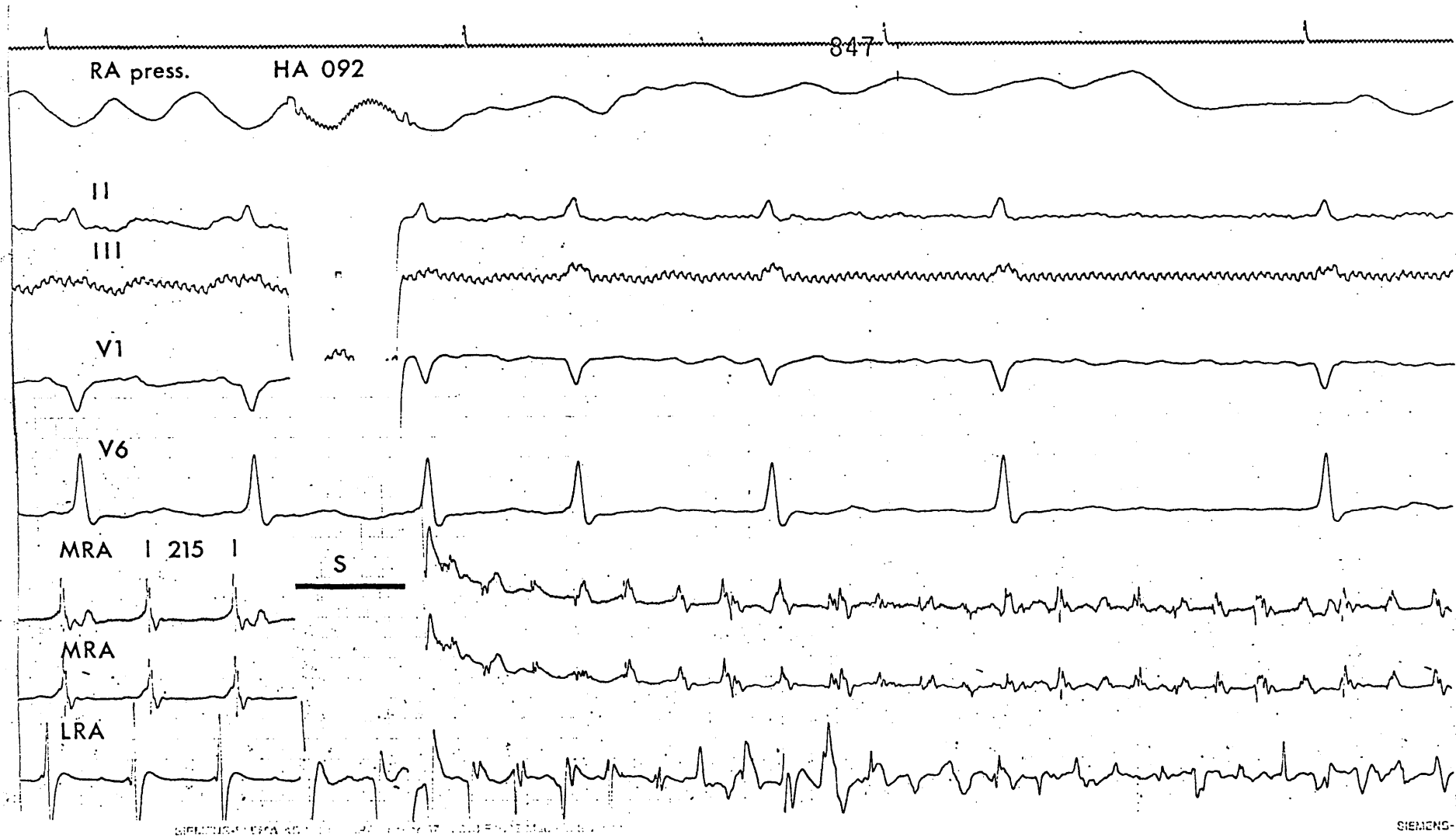


Figure 6.19

Case 62. Again, atrial fibrillation is induced by a long stimulus to the mid right atrium. The pressure trace shows loss of effective atrial contraction.

The surface traces show no regular activity, and the pressure trace becomes disorganised.

Cases 54 and 57

Figures 6.20 and 6.21 similarly show conversions to coarse fibrillation, both following Atrioverting impulses to the mid lateral atrial wall. Note in Figure 6.20 that, in the second low right atrial trace, depolarisations can be seen during the impulse. The first demonstrates that the impulse has captured. The second occurs before the end of the stimulus, and at a reduced cycle length, implying that a new circuit or focus has been set up, or that the original one has not been fully suppressed. There was no difference in the characteristics of the intra-atrial recordings between the group of patients whose atrial fibrillation was sustained, and those who reverted spontaneously to sinus rhythm.

6.5 Summary

78 Atrioversion procedures were carried out on 71 patients (53 male, 18 female; mean age 54 years). In all 78 cases, atrial flutter occurred spontaneously, and in 69 cases it was of the "common" type. Conversion was achieved in 14 patients using up to three conventional (2 ms pulse width) extrastimuli. 11 of these conversions were to sinus rhythm, and 3 to atrial fibrillation. In 6 cases, conversion to sinus rhythm was preceded by a final, flutter-like beat, whose presence may be characteristic, but is unexplained. In the remaining 64 cases who failed to convert, Atrioversion was carried out. There were 33 conversions to sinus rhythm, and 23 to atrial fibrillation. Eight cases were not affected by Atrioversion. The most important factor affecting conversion was the type of excitable window found. A Type I window was associated with 70% immediate conversion rate to sinus rhythm; a Type II produced 33% conversion (difference significant, $p < 0.005$). Analysis showed that the stimulation

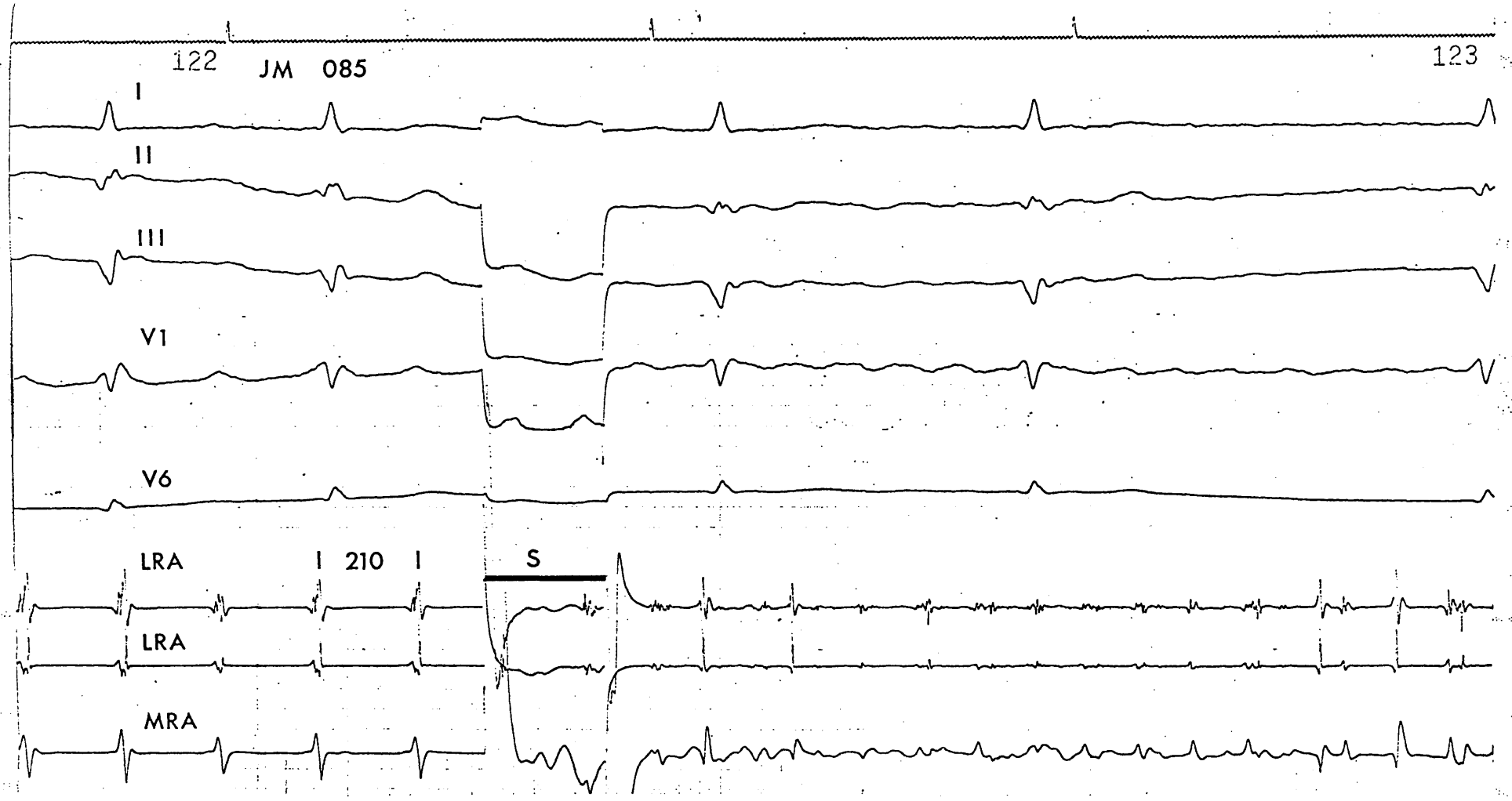


Figure 6.20

Case 55. Coarse atrial fibrillation is induced by a long stimulus. The low right atrial trace shows an electrogram during the stimulus, suggesting that effective suppression was not achieved.

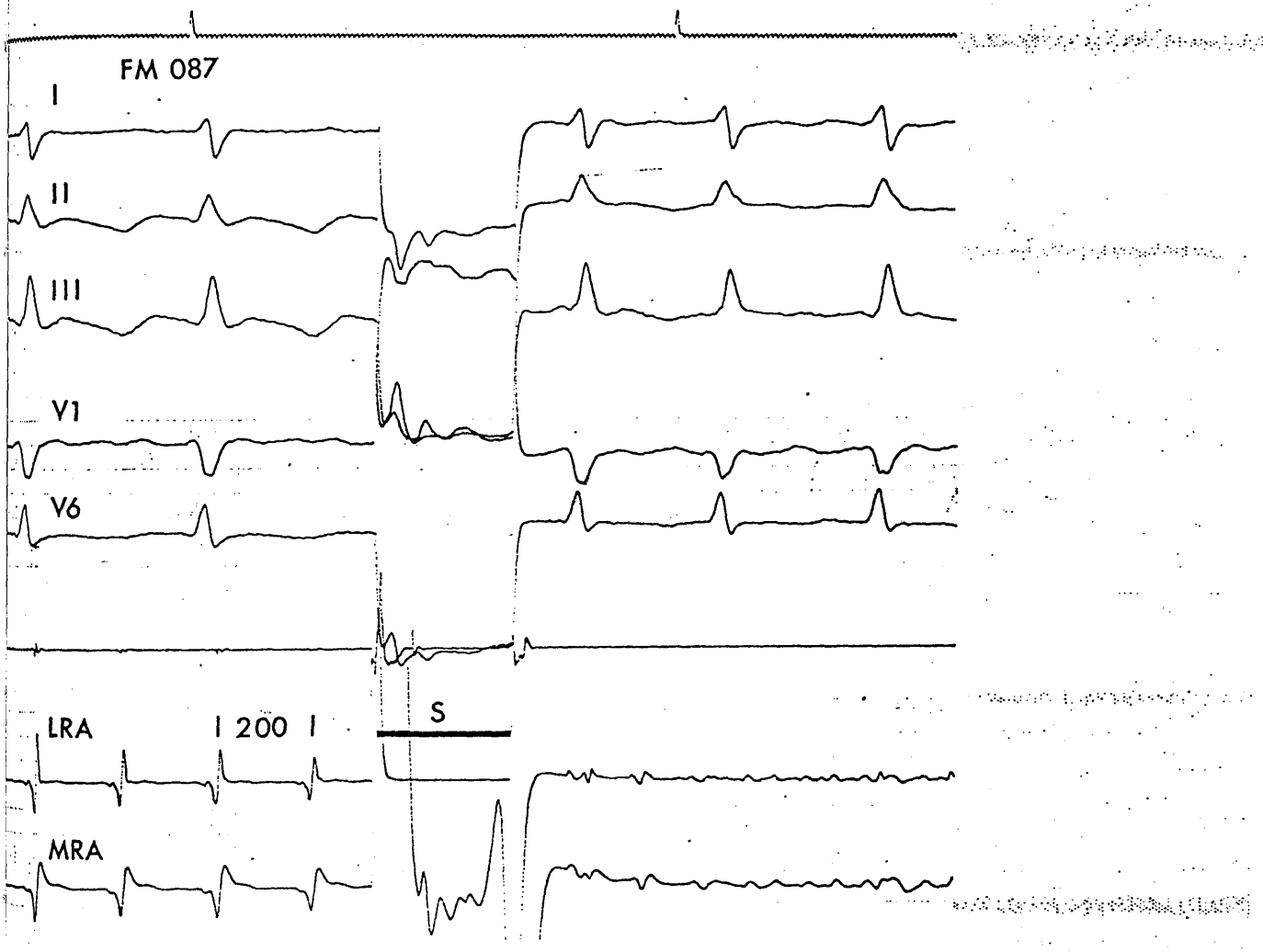


Figure 6.21

Case 57. Despite demonstrating a good Type I response in the mid right atrium, a long impulse immediately induces atrial fibrillation.

protocol described in this study is more successful than rapid atrial pacing **if a Type I response is found** ($p<0.005$).

Conversion using Atrioversion is often preceded by several irregular atrial beats, possibly associated with peripheral atrial activity returning to the area of the stimulation site, which is now no longer maintaining flutter. In some cases, this irregular beating may cause a sustained atrial fibrillation, whereas in others, it rapidly self terminates. More detailed study is required to identify precise mechanisms of conversion.

Chapter 7

A COMPUTER MODEL OF ATRIAL FLUTTER

7.1 Introduction

It has been shown in animal experiments by Allessie (1973) and Boineau (1976) that circus movement tachycardias can exist in the atria of animals, with or without anatomical obstacles. Allessie showed that a tachycardia could only be set up under favourable conditions of non-uniform refractoriness, and slowed conduction somewhere in the circuit. In addition, a critically timed and placed premature beat is required. Boineau's experiments on intact dog atria suggested that an anatomical obstacle, such as the orifice of a great vein, might also be a necessary factor in slowing conduction sufficiently to allow reentry to occur. A simple computer model of the atria was devised to test these criteria. The model incorporated the following features:

1) Pre-selectable sinus node automaticity

2) AV nodal automaticity (escape rhythm)

3) Selectable atrial conduction time and refractoriness

4) An abnormal zone with a selectable degree of slowed conduction and increased refractoriness

5) Inclusion or exclusion of inexcitable areas representing the superior and inferior venae cavae.

The model is based on a two-dimensional 18 x 18 point grid. Each point has individual conduction time and refractoriness, and can be depolarised by any

adjacent point. Once depolarised, the point cannot excite other adjacent points until its "conduction time" has elapsed. A plan of the model is shown in Figure 7.1. The atria have been opened out along the anterior inter-atrial line. No attempt has been made to incorporate conduction in the inter-atrial septum, as this would require the model to have a third dimension. The abnormal zone (IZ) is situated in the mid right atrium. The time of depolarisation of eight grid points is recorded and displayed. These points roughly correspond to commonly recorded intracardiac sites, and are : SA and AV nodes (SAN and AVN), high, mid and low right atrium (HRA, MRA and LRA), and three low left atrial sites (PCS, MCS and DCS). Note that the mid right atrial site is within the abnormal zone. The AV node activation time is displayed as HBE on the activation maps, as, in practice, it is usually estimated from a His bundle electrogram. The mean vector of depolarisation in the plane of the model is calculated at each instant in time; the horizontal, or X-component is displayed as lead I, and a combination of horizontal and vertical components is used to derive leads II and III, in identical format to the derivation of those leads on the conventional surface ECG . The display of these leads assumes that the model lies wholly in the frontal plane, which is obviously not a reasonable assumption in practice, but it allows graphic demonstration of the overall depolarisation vector in the model.

The atrial refractory period was set at 200 ms, and inter-point conduction time at 10 ms. The abnormal refractory period (ARP) was varied from 200 to 270 ms, and the abnormal conduction time varied from 10 to 70 ms. Ectopic beats were introduced initially at three sites; high right atrium, low right atrium, and low left atrium. The ectopic coupling time was varied from 210 to 270 ms, and recordings were made of the activation following the ectopic.

Activation was displayed in two ways:

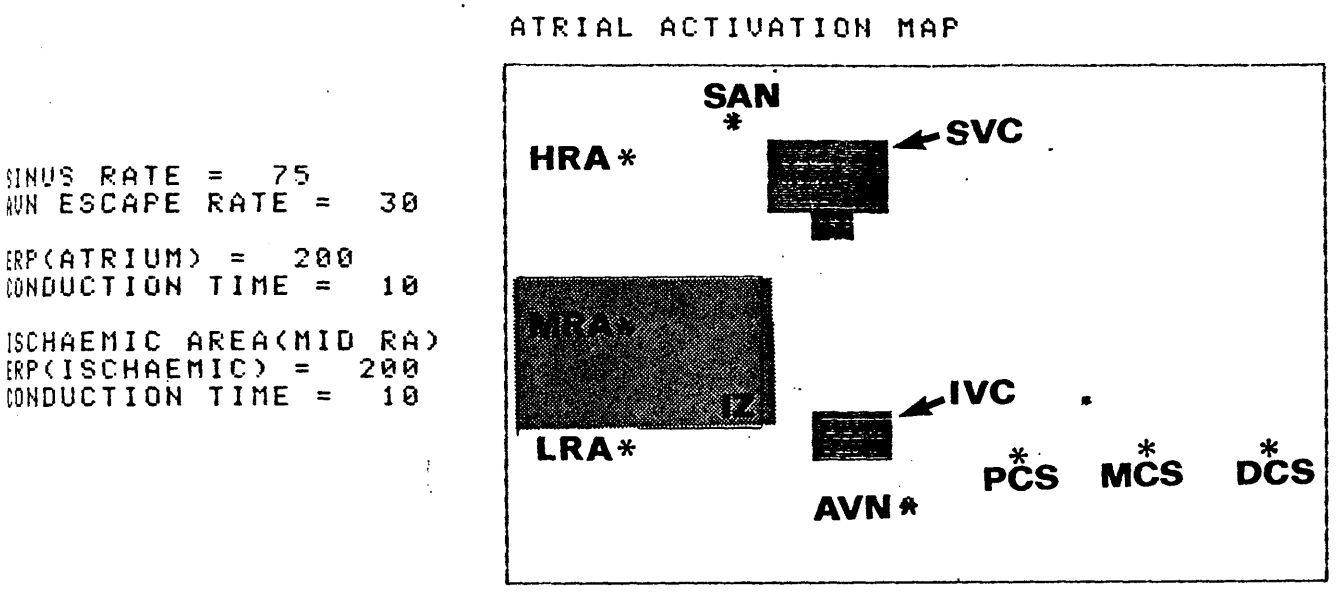


Figure 7.1

A plan of the two dimensional atrial model. Inexcitable areas (SVC, IVC) can be included. An area of slow conduction and altered refractoriness (IZ) is situated in the mid lateral "right atrium". Activation of the twelve points indicated is displayed on the electrogram map. The parameters listed on the left are standard settings, and may be altered to any desired value.

1) As a map of the grid, with refractory points marked "." and depolarising points marked "*". Excitable points are left blank.

2) As a series of "electrograms" representing activation times at the different sites, together with the derived "surface" activation leads.

7.2 Low right atrial ectopics - no anatomical obstacles

Table 7.1 shows the results obtained when ectopics were introduced in the low right atrium, and the "venae cavae" were not included in the model. It can be seen that echoes and tachycardia tended to occur when abnormal conduction was slow, and refractoriness was long. Up to three echo beats could be induced, but tachycardia only occurred with two combinations. These were ARP = 240 ms, and ACT = 50 or 70 ms. In both cases, the ectopic was coupled at the earliest possible time, namely 210 ms. Figure 7.2 shows the electrograms from the first of these tachycardias. Following a sinus beat, an ectopic is seen, and immediately a sustained tachycardia is initiated. The cycle length is 240 ms, equal to the ARP. Examination of the electrograms shows that the ectopic initially blocks between the low and mid right atria, and conduction proceeds via the AV node, returning to the mid right atrial area some 60 ms later. Figure 7.3 shows the activation maps of this tachycardia. The times on the maps are in ms, relative to the occurrence of the ectopic. It can be seen that block occurs superior to the ectopic, and activation spreads around the abnormal zone, with reentry occurring laterally at time 100 ms, and superiorly at 140 ms. Slow conduction in the abnormal zone (140 - 200 ms) allows the low atrium to recover excitability, and reentry occurs in this area at 220 ms. Figure 7.4 shows an almost identical tachycardia pattern when ACT = 70 ms. Note that the "surface" traces have a familiar undulating waveform, demonstrating that activation occurs throughout the tachycardia cycle. In Figure 7.5,

Table 7.1

LOW RIGHT ATRIAL ECTOPIC

No anatomical obstacles

Tachycardia and echo beat initiation zones:
Ranges of ectopic coupling times (ms)

Abnormal zone refractory period (ms)	**Abnormal zone conduction time(ms)**				
	30	40	50	60	70
210	**	**	**	**	**
220	**	**	**	**	**
230	**	**	**	**	**
240	**	**	210TACH	210E1	210TACH
250	**	**	210E3 220E2	210E1 220E1	210E3 220E3
260	**	210E2	210E2 220E2 230E2	210E1 220E1 230E1	210E2 220E2 230E2
270	**	210E1 220E2	210E2 220E1 230E2 240E1	210E1 220E1 230E1 240E1	210E2 220E1 230E2 240E1

Key:

** - no repetitive response
E1 - 1 echo (E2-2echoes,etc.)
TACH - sustained tachycardia

Abnormal refractory periods - 210 to 270ms (range 70ms)
Abnormal conduction times - 10 to 70ms (range 70ms)
Ectopic coupling times - 210 to 270ms (range 70ms)

Sum total of echo initiation zones = 330ms

Sum total of tachycardia zones = 20ms

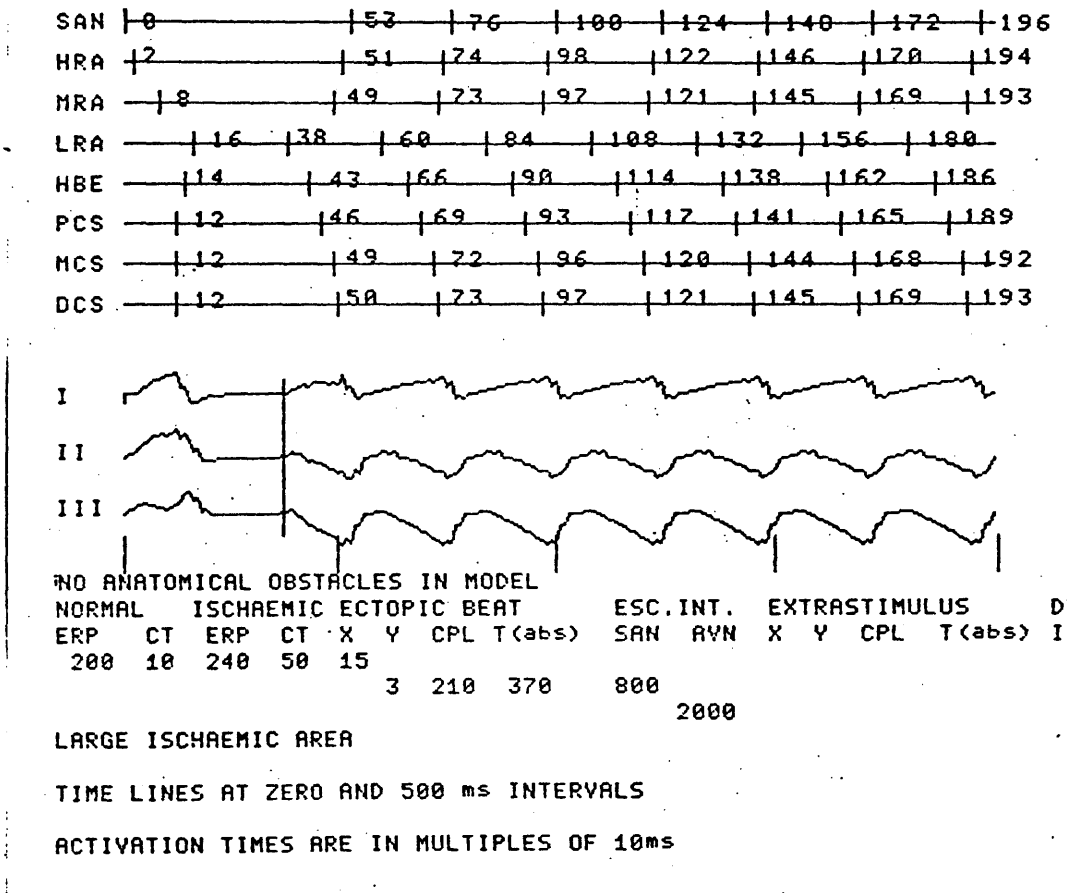


Figure 7.2

Electrogram map of a sustained tachycardia induced by a low right atrial ectopic beat. Model parameters are as shown (the right side refers to extrastimuli during tachycardia, which is not part of this discussion).

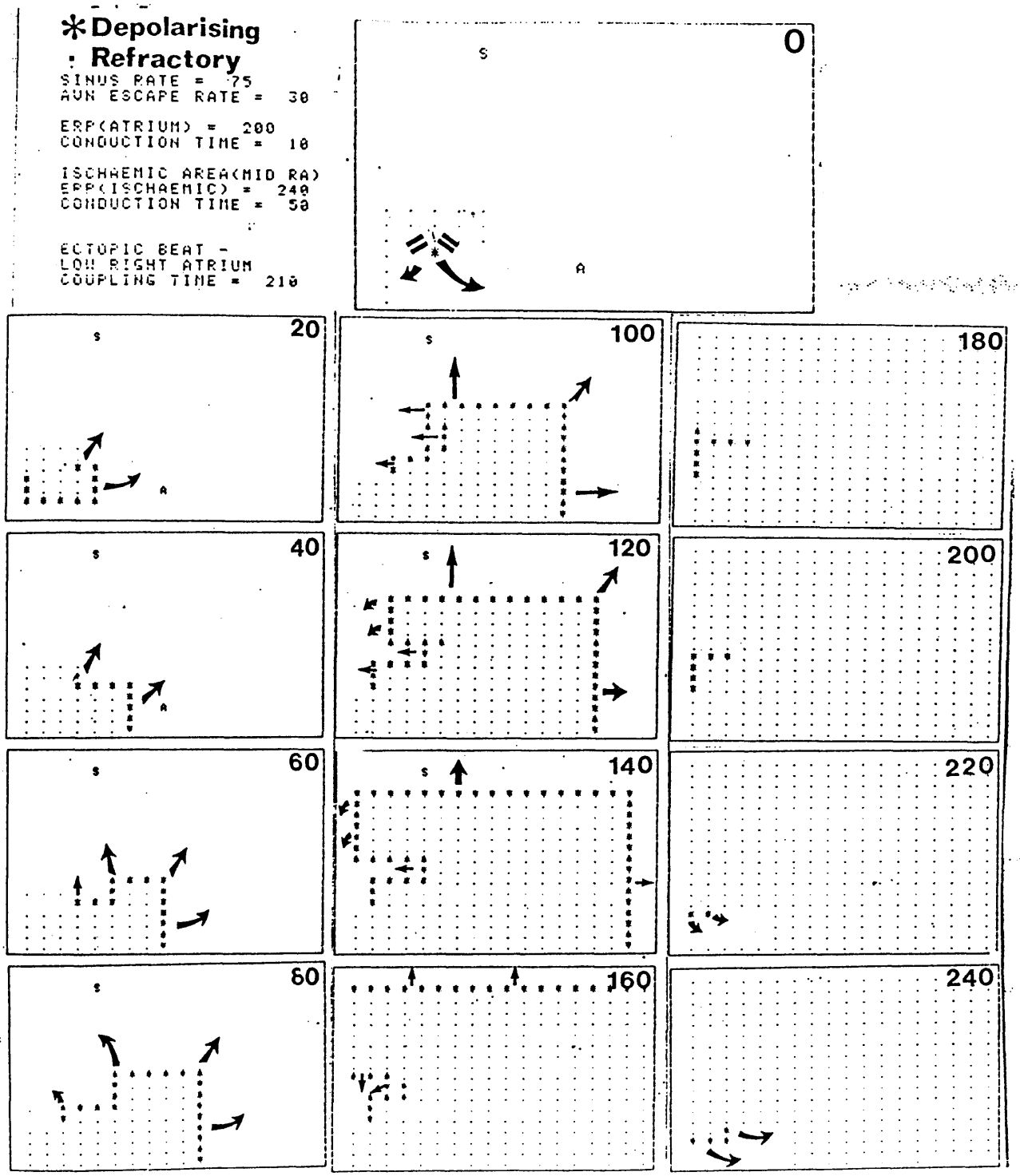


Figure 7.3

Activation maps of the tachycardia shown in Figure 7.2. Each map is labelled with a time in ms after induction of the low ectopic (large panel at top, time 0). Activation is initially blocked superiorly by the abnormal zone, with anti-clockwise spread around it (time 20 ms to 100 ms). Reentry occurs with slow conduction (120-200 ms) and eventual re-excitation of the low right atrium (220-240 ms).

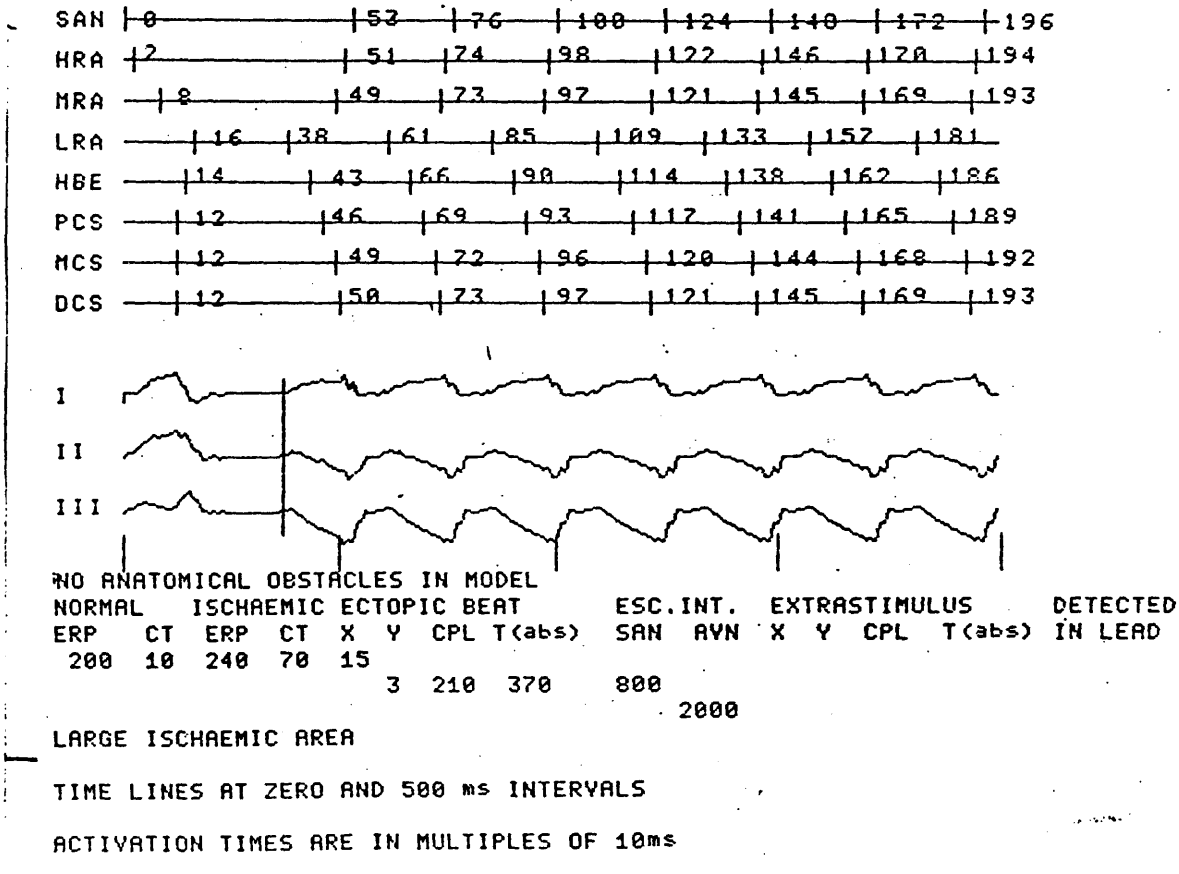


Figure 7.4

Low right atrial ectopic again induces tachycardia. The abnormal zone conduction time has been increased from 50 to 70 ms. All other parameters remain as in Figure 7.2.

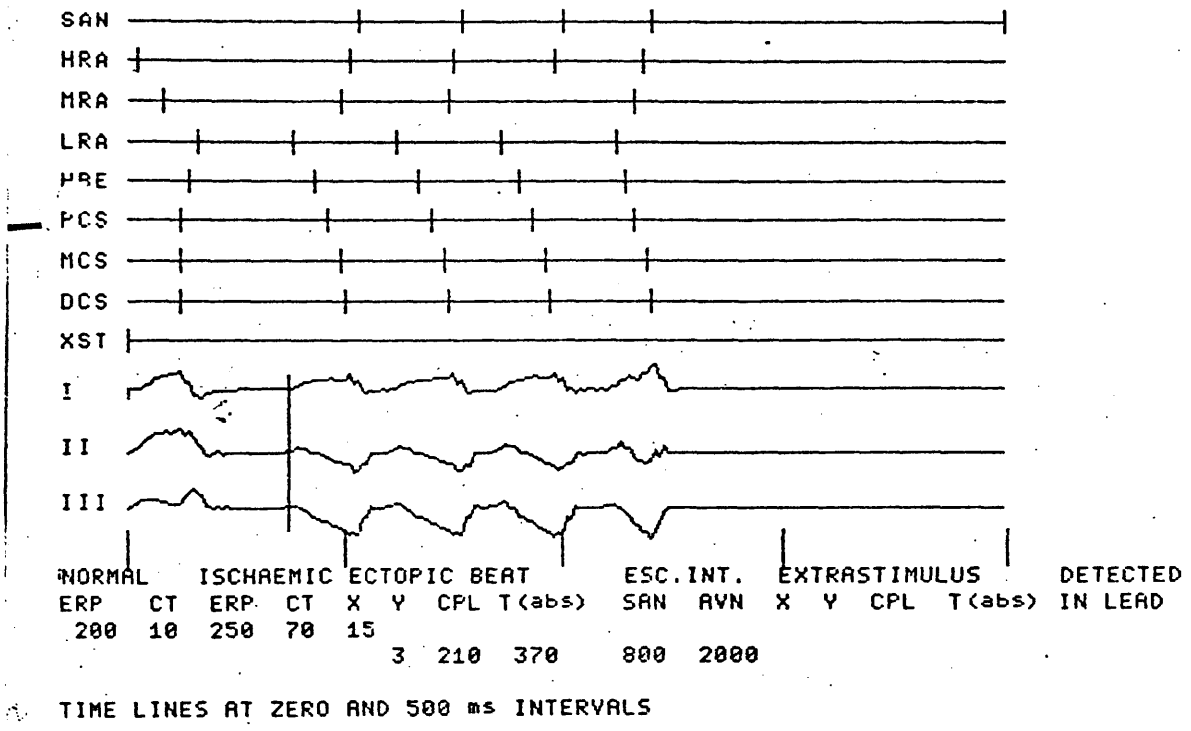


Figure 7.5

Abnormal zone refractoriness in increased by 10 ms to 250 ms. The tachycardia now self-terminates after 3 beats, illustrating the critical balance of parameters needed for maintenance of tachycardia.

lengthening of the ARP to 250 ms causes the tachycardia to self-terminate after only three echo beats. Complete block occurs in the mid right atrium during the second echo beat, and although the circus movement continues for one more beat, block again occurs, this time between the mid and low left atrial sites, and the tachycardia ceases. In Table 7.1, a sum is taken of all the echo and tachycardia initiation zones (330 ms and 20 ms respectively); these will be used as indices of the probability of tachycardia from any given ectopic site.

7.3 Low right atrial ectopics - with anatomical obstacles

Table 7.2 shows that the addition of anatomical obstacles to the model does not increase the chances of echoes or of tachycardia. The pattern is almost identical to Table 7.1, and the traces recorded are also very similar. The tachycardias induced also had cycle length equal to the abnormal refractory period. The zone sums for echoes and tachycardia are identical to Table 7.1.

7.4 High right atrial ectopics - no anatomical obstacles

When the ectopic is delivered to the high right atrium , a very different pattern emerges (see Table 7.3). Echoes and tachycardia are recorded at lower ACT and ARP values, and are much more common. These findings are reflected in the much increased zone sums for echo and tachycardia (590 and 190 ms). Tachycardia can now occur even at only slight increase in conduction time and refractoriness (ACT = 30 ms and ARP = 220 ms). Figure 7.6 shows a tachycardia which is initiated by a high right atrial ectopic. Block occurs in the mid right atrial abnormal zone, as can be seen by the missing electrogram in the MRA trace, and a tachycardia is set up, with cycle length 250 ms, which is the value of the abnormal refractory period. The "surface" electrograms show a quite different morphology from the tachycardias initiated by low ectopics. Figure 7.7 shows the spread of activation during the first cycle of

Table 7.2

LOW RIGHT ATRIAL ECTOPIC

With anatomical obstacles

Tachycardia and echo beat initiation zones:

Ranges of ectopic coupling times (ms)

Abnormal zone refractory period (ms)	Abnormal zone conduction time (ms)				
	30	40	50	60	70
210	**	**	**	**	**
220	**	**	**	**	**
230	**	**	**	**	**
240	**	**	210TACH	210E1	210TACH
250	**	**	210E3	210E1	210E3
			220E2	220E1	220E3
260	**	210E2	210E2	210E1	210E2
			220E2	220E1	220E2
			230E2	230E1	230E2
270	**	210E2	210E2	210E1	210E2
		220E1	220E1	220E1	220E1
			230E2	230E1	230E2
			240E1	240E1	240E1

Key :

** - no repetitive response
E1 - 1 echo (E2 2 echoes,etc.)
TACH - sustained tachycardia

Sum total of echo initiation zones = 330 ms

Sum total of tachycardia zones = 20 ms

Table 7.3

HIGH RIGHT ATRIAL ECTOPIC

No anatomical obstacles

Tachycardia and echo beat initiation zones:

Ranges of ectopic coupling times (ms)

Abnormal zone refractory period (ms)	Abnormal zone conduction time (ms)				
	30	40	50	60	70
210	**	**	**	**	**
220	210TACH	210TACH	210TACH	210TACH	210TACH
230	210E3	210TACH	210TACH	210E2	210TACH
	220E3	220TACH	220TACH	220E2	220TACH
240	210E1	210E1	210E1	210E1	210TACH
	220E2	220E2	220TACH	220E1	220TACH
	230E2	230E2	230TACH	230E1	230TACH
250	220E1	220E1	220E1	220E1	220E1
	230E2	230E2	230E2	230E1	230TACH
	240E2	240E2	240E2	240E1	240TACH
260	220E1				
	230E1	230E1			
	240E2	240E2	240E1	240E1	240E1
					250E1
270	230E1				
	240E1	240E1			
					250E1
					260E1

Key :

** - no repetitive response
E1 - 1 echo (E2 - 2 echoes,etc.)
TACH - sustained tachycardia

Sum total of echo initiation zones = 590 ms

Sum total of tachycardia zones = 190 ms

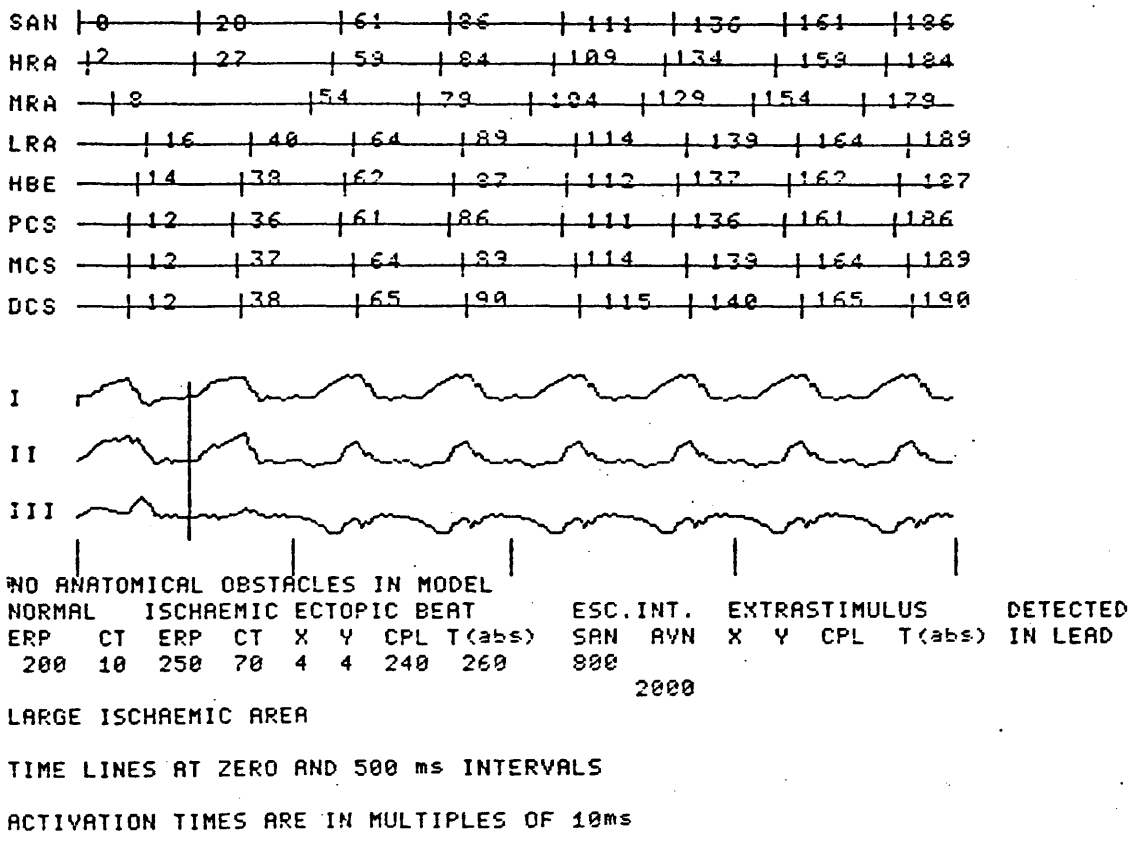


Figure 7.6

A tachycardia induced by a high right atrial ectopic. The cycle length is identical to the abnormal zone refractory period. The derived "surface" leads show a quite different morphology to tachycardia induced by low atrial ectopics.

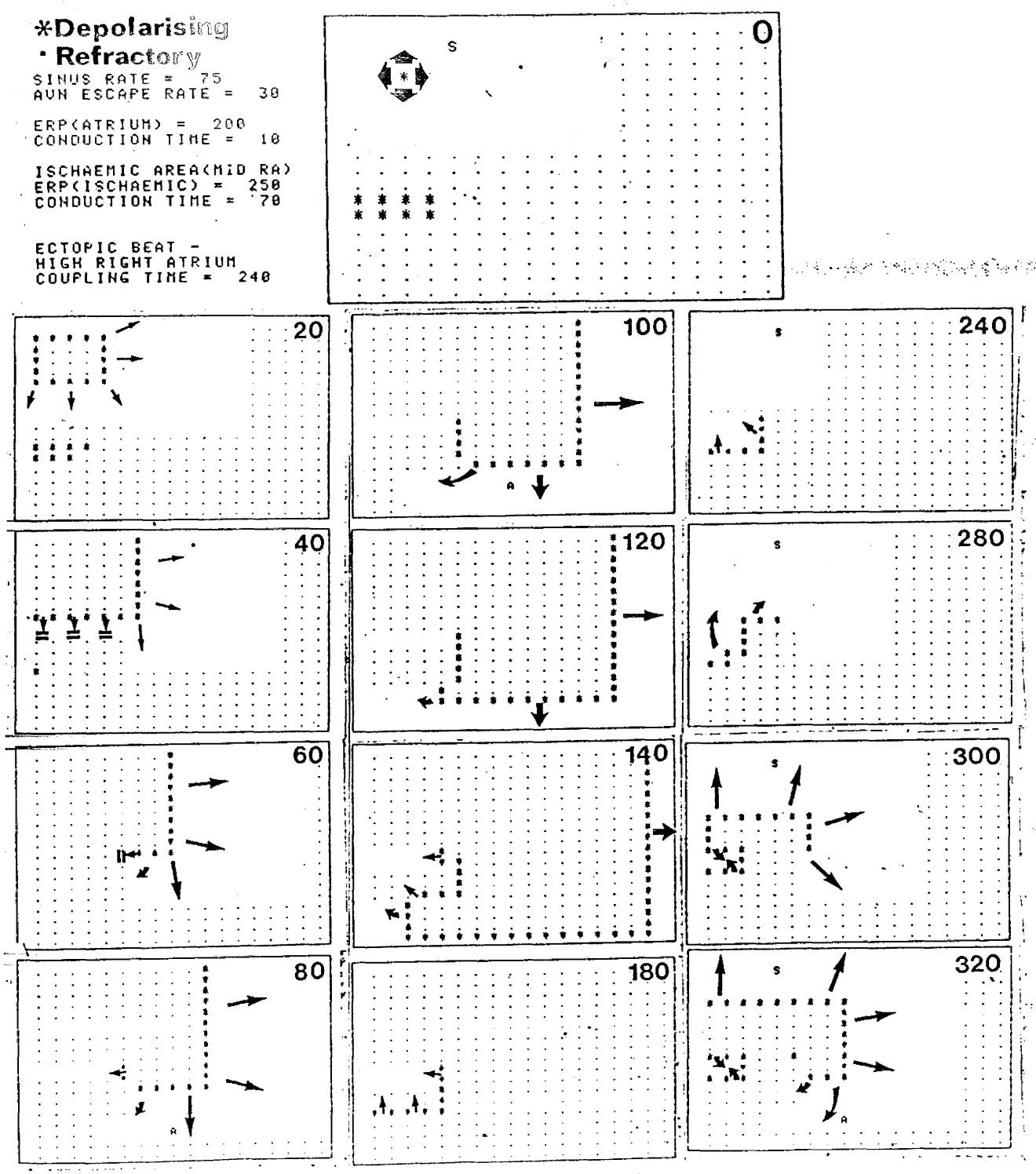


Figure 7.7

Activation maps for tachycardia of Figure 7.6. High atrial ectopic (time 0) blocks in the abnormal zone, and circulates clockwise in the excitable tissue around this zone (60-140 ms). Reentry occurs at the lateral and inferior borders of the abnormal zone, and slowed conduction allows re-excitation of the high right atrium, setting up tachycardia.

this tachycardia. Block occurs at time 40 ms, in the mid right atrium, and the impulse circumvents this area, reentering laterally at 80 ms and inferiorly at 140 ms. By time 280 ms, the normal atrial tissue has recovered, and is depolarised again. There are small opposing wavefronts in the abnormal zone at 300 ms, but these collide and extinguish, and do not prevent reentry during the next cycle. The tachycardia has a clockwise activation path in the plane of the model, in contrast to the anti-clockwise path seen in Figure 7.3.

7.5 High right atrial ectopics - with anatomical obstacles

The introduction of venae cavae into the model reduces the likelihood of echo beats or tachycardia following high right atrial ectopics, as is seen in Table 7.4. Both echo and tachycardia zone sums are reduced by 50 ms. The reason for this small reduction in incidence appears to be due to the delay in conduction around the obstacles, which allows the abnormal zone to recover excitability too early, and hence opposing wavefronts are set up in the circuit which collide, terminating the tachycardia. An example of this is seen in Figure 7.8. Here, the refractory periods, conduction times and ectopic coupling time are identical to the tachycardia in Figure 7.6, but the introduction of anatomical obstacles reduces the response to two echo beats. Close examination shows that block occurs between low and mid right atrium. The high right atrial trace is slightly delayed due to the venae cavae, and competitive depolarisation of the abnormal zone has occurred from the superior and inferior directions, resulting in cancellation of the impulse.

7.6 Low left atrial ectopics

There were no echo beats or tachycardia from any combination of parameters, following a low left atrial ectopic. The reason for this occurrence is the distance between the ectopic site and the abnormal zone. Either the ectopic reaches this zone from both sides simultaneously, and bidirectional block

Table 7.4

HIGH RIGHT ATRIAL ECTOPIC

With anatomical obstacles

Tachycardia and echo beat initiation zones:

Ranges of ectopic coupling times (ms)

Abnormal zone refractory period (ms)	**Abnormal zone conduction time (ms)**				
	30	40	50	60	70
210	**	**	**	**	**
220	**210TACH**	**210TACH**	**210TACH**	**210TACH**	**210TACH**
230	210E2	**220TACH**	**210TACH**	210E1	**210TACH**
	220E3	**220TACH**	**220TACH**	220E1	**220TACH**
240	210E1	210E1			
	220E2	220E2	**220TACH**	220E1	**220TACH**
	230E2	230E2	**230TACH**	230E1	**230TACH**
250	210E1				
	220E1	220E1			
	230E2	230E2	230E2	230E1	230E1
	240E2	240E2	240E2	240E1	240E2
260	220E1				
	230E1	230E1			
	240E2	240E2	240E1	240E1	240E1
					250E1
270	230E1				
	240E1	240E1			
					250E1
					260E1

Key :

** - no repetitive response
E1 - 1 echo (E2 - 2 echoes,etc.)
TACH - sustained tachycardia

Sum total of echo initiation zones = 540 ms

Sum total of tachycardia zones = 150 ms

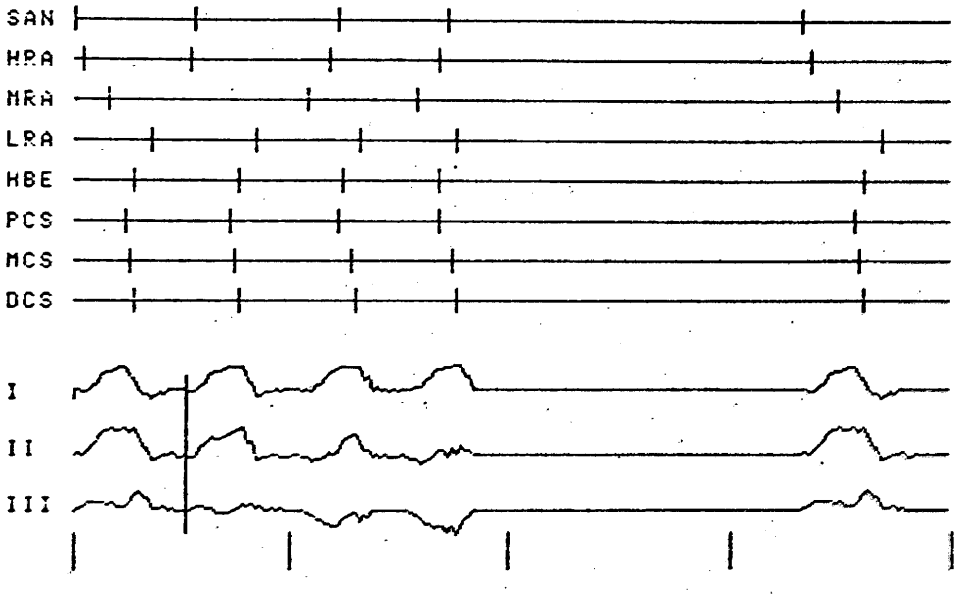


Figure 7.8

All parameters are identical to those used in Figures 7.6 and 7.7, but anatomical obstacles have been included. Tachycardia is not induced, and only two echo beats follow the ectopic impulse.

occurs, or the transit time from ectopic site to abnormal zone is greater than the difference in refractory periods, and no block occurs.

7.7 Summary

This model has obvious limitations in terms of physiological accuracy, for instance in its grossly over-simplified two dimensional form, without "wrap-over" conduction at the edges, and in its failure to alter the refractory periods of the tissues in response to echo beats or tachycardia, as would occur physiologically in the human atrium. Nevertheless, it illustrates several points, in agreement with the animal experiments carried out by Allessie.

1) It is possible to sustain a tachycardia in a mass of "tissue" without anatomically defined reentrant pathways.

2) Tachycardia initiation depends on non-uniform refractoriness and slowed conduction.

3) A precisely timed and placed ectopic beat is necessary for initiation.

4) The tachycardia cycle length is dependent on the tissue refractory period.

In addition, several other points are suggested by this model.

5) It may not always be the most premature ectopic beats which initiate tachycardia. Sometimes slightly later beats may be more effective.

6) The introduction of anatomical obstacles can, in some instances, introduce too much conduction delay, and prevent tachycardia initiation, rather than facilitate it.

In vitro studies may be required show whether these last two points can ever be applied to clinically occurring atrial flutter.

Chapter 8

CONCLUSIONS

8.1 The mechanism of atrial flutter

The present study strongly suggests that atrial flutter in man is due to a macro-reentrant circuit, often involving some, but not all of the right atrium. In eight patients, multiple Type I responses were observed at atrial sites with different activation times. Furthermore, the differences in activation were sufficiently large to preclude such Type I responses occurring in the presence of an automatic focus. The reentrant circuit appears to have a variable location; in some patients, a Type I response can be found at a given atrial site, where in others the same or closely similar site shows a Type II response. High right atrial sites often show such variability, while low lateral sites more consistently show a Type I response. Presumably, the intra-atrial circuit more often includes the low than the high atrium. The exact nature of the obstacle around which the wavefront circulates cannot be determined from the small number of recording sites possible; anatomical, functional or a combination of both types of block are possible.

Atrial endocardial mapping during flutter revealed inconsistent activation patterns, despite apparently concordant surface ECG atrial activity in different patients. Fragmented and split potentials were found most often in the mid to low anterolateral right atrium, where a Type I response was also most likely to be found.

8.2 Conversion of atrial flutter using Atrioversion

This study has looked at the use of a new technique of electrical stimulation for the termination of atrial flutter. The technique of Atrioversion uses a single, timed, long constant current pulse, in an attempt to convert atrial flutter to sinus rhythm. In 78 cases of spontaneously occurring atrial flutter in man, the

overall success rate of Atrioversion was shown to be comparable to that of rapid atrial pacing. In addition, successful conversion could be facilitated by careful positioning of the electrode catheter, at an atrial site where conventional extrastimuli during atrial flutter were followed by non-compensatory pauses (Type I response). Type I atrial sites were associated with a 71% conversion rate to sinus rhythm, which was significantly higher than Type II sites (33%). Conversion to sinus rhythm at Type I sites was also significantly more likely than with rapid atrial pacing (from data pooled from the literature).

Conversion rate using combinations of conventional extrastimuli in atrial flutter was low (15%), but still higher than found in most other studies. This probably reflects the high degree of care taken to explore various stimulation sites in this study.

The mechanism of conversion using Atrioversion is not clear. It is possible that the continued passage of electrical current exerts an electrotonic effect upon the atrial cells at the stimulation site, and holds this site in a depolarised, refractory state for the duration of the impulse. If the site is within a reentry circuit, termination of the circulating impulse could result. It is also possible that the long stimulus causes conversion by induction of multiple extrastimuli, due to the fact that the underlying tissue is depolarised by the leading edge of the pulse, and then is stimulated again by the constant current pulse as soon as it becomes excitable - the long pulse thereby acting as an automatic paired (or triple) stimulus.

Atrial fibrillation may be induced; in some patients spontaneous reversion to sinus rhythm occurs after several hours, and sometimes AF is sustained indefinitely.

Conversion of atrial flutter to sinus rhythm is normally followed by several rapid, irregular atrial beats. This may reflect the large portion of the atria not directly involved in the reentry circuit, but passively depolarised from it.

8.3 Limitations of the study and future work

The present study was limited in its conclusions by several factors. Early in the series, technological limitations did not allow simultaneous multiple site mapping during flutter. Latterly, multiple electrograms could be recorded, but as with all electrophysiological studies, endocardial mapping is of limited value in defining arrhythmia mechanisms. An accurate estimation of activation patterns would have been possible in a reproducible animal model of flutter, and would have allowed more accurate estimation of factors affecting successful Atrioversion, by allowing comparison of several conversion attempts within each animal. The actual mechanism of conversion remains uncertain, and needs to be clarified by cellular electrophysiological studies.

A further limitation lay in the fact that all cases were spontaneously occurring flutter, and the primary objective was restoration of sinus rhythm. If induction studies were performed, multiple episodes of flutter could be obtained in each patient, and a definitive estimation of the importance of various parameters (such as pulse width and amplitude) on conversion could be made. In addition, an accurate within-patient comparison of Atrioversion against rapid atrial pacing could be made. It would be of value to perform all of these further studies.

Further work will be carried out to clarify the potential role of the long pulse in the conversion of other arrhythmias, particularly ventricular tachycardia, where a single stimulus conversion would be most useful (thus avoiding the risk of the rhythm deteriorating to ventricular fibrillation, due to haemodynamic intolerance).

Successful termination of rapid ventricular tachycardia would be a considerable advantage, and might suggest the use of the technique in implantable devices, as part of a hierarchical approach to conversion of malignant ventricular arrhythmias.

References

Alexander S, Kleiger R, Lown B. Use of external electric countershock in the treatment of ventricular tachycardia. JAMA. 177:916, 1961.

Allessie MA, Bonke FIM, Schopman FJG. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. Circ Res. 33:54, 1973.

Allessie MA, Bonke FIM, Schopman FJG. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. II. The role of nonuniform recovery of excitability in the occurrence of unidirectional block, as studied with multiple microelectrodes. Circ Res. 39:168,1976.

Allessie MA, Bonke FIM, Schopman FJG. Circus movement in rabbit atrial muscle as a mechanism of tachycardia. III. The "leading circle" concept: a new model of circus movement in cardiac tissue without the involvement of an anatomical obstacle. Circ Res. 41:9, 1977.

Allessie MA, Lammers WJEP, Bonke FIM, Hollen J. Intra-atrial reentry as a mechanism for atrial flutter induced by acetylcholine and rapid pacing in the dog. Circulation. 70:123, 1984.

Allessie MA, Lammers WJEP, Bonke FIM, Hollen J. Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation. In: Cardiac electrophysiology and arrhythmias. Eds: Zipes DP, Jalife J. Grune and Stratton. Orlando, 1985.

Bertholet M, Hastir F, Kassab A, et.al. Synchronized increasing train stimulation for management of type I atrial flutter. Am J Cardiol. 57:341, 1986.

Boineau JP, Mooney CR, Hudson RD, Hughes DC, Erdin RA, Wylds AC. Observations on reentrant excitation pathways and refractory period distributions in spontaneous and experimental atrial flutter in the dog. In: Reentrant Arrhythmias. Ed. Kulbertus HE. Baltimore. University Park Press, 1976.

Boineau JP, Schuessler RB, Mooney CR, et al. Natural and evoked atrial flutter due to circus movement in dogs. Role of abnormal atrial pathways slow conduction, nonuniform refractory period distribution and premature beats. Am J Cardiol. 45:1167, 1980.

Braunwald E. Heart disease. A textbook of cardiovascular medicine. Philadelphia. WB Saunders, 1980.

Cabrera CE, Sodi-Pallares D. Discusion del movimiento circular y prueba directa de su existencia en el flutter auricular clinico. Arch Inst Cardiol Mex. 17:850, 1947.

Camm AJ, Ward DE, Spurrell RAJ. Response of atrial flutter to overdrive atrial pacing and intravenous disopyramide phosphate singly and in combination. Br Heart J. 44:240, 1980.

Camm AJ, Ward DE. Antiarrhythmic drugs (2). Hospital Update.1283 December, 1981.

Cheng TO. Rapid atrial pacing in treatment of atrial flutter and atrial tachycardia. Clin Res. 19:307, 1971.

Cosio FG, Arribas F, Palacios J, Tascon J, Lopez-Gil M. Fragmented electrograms and continuous electrical activity in atrial flutter. Am J Cardiol. 57:1309, 1986.

Das G, Anand MK, Ankineedu K, Chinnavaso T, Talmers FN, Weissler AM. Atrial pacing for cardioversion of atrial flutter in digitalized patients. Am J Cardiol. 41:308, 1978.

Disertori M, Inama G, Vergara G, Guarnerio M, del Favero A, Furlanello F. Evidence of a reentry circuit in the common type of atrial flutter in man. Circulation. 67:434, 1983.

Einthoven W. Ein neues Galvanometer. Ann Phys Lpz 12:1059, 1903.

Evans GT, Scheinman MM. The percutaneous cardiac mapping and ablation registry: summary of results. PACE. 9:923, 1986.

Fisher JD. Role of electrophysiologic testing in the diagnosis and treatment of patients with known and suspected bradycardias and tachycardias. Prog Cardiovasc Dis. 24:25, 1981.

Friedman PL, Brugada P, Kuck K-H, Roy D, Farre J, Bar FWHM, Wellens HJJ. Inter- and intraatrial dissociation during spontaneous atrial flutter: Evidence for a focal origin of the arrhythmia. Am J Cardiol. 50:756, 1982.

Gloor HO, Fromer M, Kappenberger LJ. Endocardial conversion of atrial flutter: success rate of various stimulation protocols. Clin Prog Electrophysiol Pacing. 4:67,1986.

Goy J-J, Grbic M, Hurni M, et al. Conversion of supraventricular arrhythmias to sinus rhythm using flecainide. Eur Heart J. 6:518, 1985.

Gulotta SJ, Aronson AL. Cardioversion of atrial tachycardias and flutter by atrial stimulation. Am J Cardiol. 26:262, 1970.

Haft JI, Kosowksy BD, Lau SH, Stein E, Damato AN. Termination of atrial flutter by rapid electrical pacing of the atrium. Am J Cardiol. 20:239, 1967.

Hayden WG, Hurley EJ, Rytand DA. The mechanism of canine atrial flutter. Circ Res. 20:496, 1967.

Henthorn R, Roberts WS, Kelly K, Leier CV. Conversion of atrial flutter: rapid atrial pacing as a bedside technique. PACE. 3:202, 1980.

Hoffmann BF, Cranefield PF. Electrophysiology of the heart. New York. McGraw-Hill, 1960.

Hoffmann BF, Cranefield PF. The physiological basis of cardiac arrhythmias. Am J Med. 37:670, 1964.

Hooker DR, Kouwenhoven WB, Langworthy OR. Effect of alternating electrical currents on the heart. Am J Physiol. 103:444, 1933.

Inoue H, Matsuo H, Takayanagi K, Murao S. Clinical and experimental studies of the effects of atrial extrastimulation and rapid pacing on atrial flutter cycle: evidence of macro reentry with an excitable gap. Am J Cardiol. 48:623, 1981.

Jackson WM, Zipes DP. Transvenous low-energy cardioversion of ventricular tachycardia in a canine model of subacute myocardial infarction (abstr). Circulation. July, 1982.

Jolly WA, Ritchie WT. Auricular flutter and fibrillation. Heart 2:177, 1911.

Josephson ME, Seides SF, Batsford WB, Caracta AR, Damato AN, Kastor JA. The effects of carotid sinus pressure in reentrant paroxysmal supraventricular tachycardia. Am Heart J. 88:694, 1974.

Josephson ME, Seides SF. Clinical cardiac electrophysiology. Techniques and interpretations. Philadelphia. Lea and Febiger, 1979.

Kato K, Sato M, Harumi K, Sakamoto T, Koyama S, Murao S. Studies on auricular flutter. Observations upon F wave. Resp Circ. 5:837, 1957.

Katz LN, Pick A. Current status of theories of mechanisms of atrial tachycardias flutter and fibrillation. Prog Cardiovasc Dis. 2:650, 1959.

Kerr CR, Gallagher JJ, Smith WM, Sterba R, German LD, Cook L, Kasell JH. The induction of atrial flutter and fibrillation and the termination of atrial flutter by esophageal pacing. PACE. 6:60, 1983.

Kimura E, Kato K, Murao S, Ajisaka H, Koyama S, Omiya Z. Experimental studies on the mechanism of the auricular flutter. Tohoku J Exp Med. 60:197, 1954.

Klein GJ, Guiraudon GM, Sharma AD, Milstein S. Demonstration of macroreentry and feasibility of operative therapy in the common type of atrial flutter. Am J Cardiol. 57:587, 1986.

Lanari A, Lambertini A, Ravin A. Mechanism of experimental atrial flutter. Circ Res. 4:282, 1956.

Lemberg L, Castellanos A, Swenson J, Gosselin A. Arrhythmias related to cardioversion. Circulation. 30:163, 1964.

Lerman BB, Deale OC, Clark CW. A resistive network model for intrathoracic current pathways during transthoracic defibrillation. Circulation. 74:II-341, 1986.

Lewis T, Feil HS, Stroud WD. Observations upon flutter and fibrillation. Part II - the nature of auricular flutter. Heart 7:191, 1920.

Lewis T. Observations upon flutter and fibrillation. Part IV - impure flutter theory of circus movement. Heart. 7:293, 1920.

Lewis T, Drury AN, Iliescu CC. A demonstration of circus movement in clinical flutter of the auricles. Heart. 8:341, 1921.

Lewis T. The mechanism and graphic registration of the heart beat 3rd ed. London Shaw & sons Ltd., 1925.

Lister JW, Cohn LS, Bernstein WH, Samet P. Treatment of supraventricular tachycardias by rapid atrial stimulation. Circulation. 38:1044, 1968.

Lown B, Amarasingham R, Neuman J. New method for terminating cardiac arrhythmias: use of synchronized capacitor discharge. JAMA. 182:548, 1962.

Lown B, Kaid Bey S, Perlroth M, Abe T. Cardioversion of ectopic tachycardias. Am J Med Sciences. 257 September, 1963.

Lown B. "Cardioversion" of arrhythmias (I). Modern concepts of cardiovascular disease. 33:863, 1964.

Marques MG, Motta JCB, Nogueira RA. The mechanism of atrial flutter. Cardiologia. 40:269, 1962.

Massumi RA, Kistin AD, Tawakkol AA. Termination of reciprocating tachycardia by atrial stimulation. Circulation. 36:637, 1967.

Mayer AG. Rhythmical pulsations in scyphomedusae. Carnegie Institution Publication. 47:1, 1906.

Mines GR. On dynamic equilibrium in the heart. J Physiol (London). 46:349, 1913.

Mirowski M, Alkan WJ. Left atrial impulse formation in atrial flutter. Brit Heart J. 29:299, 1967.

Mirowski M, Mower MM, Gott VL, Brawley RK. Feasibility and effectiveness of low-energy catheter defibrillation in man. Circulation. 47:79, 1973.

Mirowski M, Reid PR, Mower MM, et al. Termination of malignant ventricular arrhythmias with an implanted automatic defibrillator in human beings. N Engl J Med. 303:322, 1980.

Mitsui T, Tanaka T, Saigusa M. An esophageal balloon electrode for cardiac pacing. In: Cardiac pacing. Ed. Thalen HJT. Assen The Netherlands. Van Gorcum & Co, 1973.

Moe GK. On the multiple wavelet hypothesis of atrial fibrillation. Arch Int Pharmacodyn Therapy. 140:183, 1962.

Montoyo JV, Angel J, Valle V, et al. Cardioversion of tachycardias by transesophageal pacing. Am J Cardiol. 32:85, 1973.

Murphy B, Lewis HD, Brymer J. Atrial flutter: termination by rapid atrial pacing. J Kans Med Soc. 79:666, 1979.

Oram S, Davis JPH, Weinbren I, Taggart P, Kitchen LD. Conversion of atrial fibrillation to sinus rhythm by direct current shock. Lancet. 2:159, 1963.

Orlando J, Cassidy J, Aronow WS. High reversion of atrial flutter to sinus rhythm after atrial pacing in patients with pulmonary disease. Chest. 71:580, 1977.

Pastelin G, Mendez R, Moe GK. Participation of atrial specialized conduction pathways in atrial flutter. Circ Res. 42:386, 1978.

Pittman DE, Makar JS, Kooros KS, Joyner CR. Rapid atrial stimulation: successful method of conversion of atrial flutter. Am J Cardiol. 32:700, 1973.

Plumb VJ, James TN, Waldo AL. Evidence that atrial flutter is due to a circus movement with an excitable gap. Circulation. 62(Supp III):46, 1980.

Preston TA. Atrial pacing to convert atrial flutter (letter). Am J Cardiol. 32:737, 1973.

Prevost JL, Battelli F. La mort par les courants electriques: courants alternatif a haute tension. J Physiol et Path Gen. 1:427, 1899.

Prinzmetal M, Corday E, Brill IC, Oblath RW, Kruger HE. The auricular arrhythmias. Springfield Ill. Charles C Thomas, 1952.

Puech P, Latour H, Grolleau R. Le flutter et ses limites. Arch Mal Coeur. 63:116, 1970.

Puech P, Grolleau R, Latour H, Cabasson J, Robin JM, Baissus C. Traitement du flutter auriculaire par la stimulation auriculaire endocavitaire. Arch Mal Coeur. 66:159, 1973.

Rosen KM, Lau SH, Damato AN. Simulation of atrial flutter by rapid coronary sinus pacing. Am Heart J. 78:635, 1969.

Rosen KM, Sinno MZ, Gunnar RM, Rahimtoola SH. Failure of rapid atrial pacing in the conversion of atrial flutter. Am J Cardiol. 29:524, 1972.

Rosenblueth A, Garcia Ramos J. Studies on flutter and fibrillation. II. The influence of artificial obstacles on experimental auricular flutter. Am Heart J. 33:677, 1947.

Rytand DA. The circus movement (Entrapped circuit wave) hypothesis and atrial flutter. Ann Intern Med. 65:125, 1966.

Scheinman MM, Morady F, Hess S, Gonzalez R. Catheter-induced ablation of the atrioventricular junction to control refractory supraventricular arrhythmias. JAMA. 248:851, 1982.

Scherf D. Versuche zur theorie des vorhofflatterns und vorhofflimmerns. Z Ges Exp Med. 61:30, 1928.

Scherf D. Studies on auricular tachycardia caused by aconitine administration. Proc Soc Exp Biol. 64:233, 1947.

Scherf D, Blumenfeld S. Mechanism of auricular flutter caused by crushing and electric stimulation. Cardiologia. 24:193, 1954.

Scherf D, Blumenfeld S, Taner D, Yildiz M. The effects of diphenylhydantoin (Dilantin) sodium on atrial flutter and fibrillation provoked by focal application of aconitine or delphinine. Am Heart J. 60:936, 1960.

Scherf D. The mechanism of flutter and fibrillation. Am Heart J. 71:273, 1966.

Strasberg B, Sclarovsky S, Kusniec J, Agmon J. Oral and intravenous amiodarone for atrial fibrillation/flutter. Clin Prog Electrophysiol Pacing. 4:508,1986.

Sung RJ, Waxman HL, Elser B, Juma Z. Treatment of paroxysmal supraventricular tachycardia and atrial flutter-fibrillation with intravenous verapamil: efficacy and mechanism of action. Clin Invest Med. 3:41, 1980.

Ten Eick RE, Wyte SE, Ross SM, Hoffman BF. Post-countershock arrhythmias in untreated and digitalized dogs. Circ Res. 13:21, 1963.

Vaughan-Williams EM. Classification of antiarrhythmic drugs. In: Symposium on cardiac arrhythmias Elsinore, Denmark. Ed Sandoe E Flensted-Jensene E, Olessen KH. Sodertalje. AB Astra, 1970.

Vergara GS, Hildner FJ, Schoenfeld CB, Javier RP, Cohen LS, Samet P. Conversion of supraventricular tachycardias with rapid atrial stimulation. Circulation. 46:788, 1972.

Waldo AL, MacLean WAH, Karp RB, Kouchoukos NT, James TN. Entrainment and interruption of atrial flutter with atrial pacing: studies in man following open heart surgery. Circulation. 56:737, 1977.

Watson RM, Josephson ME. Atrial flutter. I. Electrophysiologic substrates and modes of initiation and termination. Am J Cardiol. 45:732, 1980.

Waxman MB, Wald RW, Sharma AD, Huerta Ad, Cameron DA. Vagal techniques for termination of paroxysmal supraventricular tachycardia. Am J Cardiol. 46:655, 1980.

Wellens HJJ, Janse MJ, van Dam RT, Durrer D. Epicardial excitation of the atria in a patient with atrial flutter. Brit Heart J. 33:233, 1971.

Wellens HJJ. Contribution of cardiac pacing to our understanding of the Wolff-Parkinson-White syndrome.Br Heart J. 37:321, 1975.

Wellens HJJ. Electrical management of arrhythmias with emphasis on the tachycardias. Am J Cardiol. 41:1025, 1978.

Wellens HJJ. Role of cardiac electrical stimulation techniques in the diagnosis and therapy of cardiac arrhythmias: clinical aspects. In: Cardiac pacing. Eds. Samet P El-Sherif N. Grune & Stratton, 1980.

Wells JL, MacLean WAH, James TN, Waldo AL. Characterization of atrial flutter: studies in man after open heart surgery using fixed atrial electrodes. Circulation. 60:665, 1979.

Wiggers CJ. Physiologic basis for cardiac resuscitation from ventricular fibrillation: method for serial defibrillation. Am Heart J. 20:413, 1940.

Wilson FN, MacLeod AG, Barker PS. The distribution of the currents of action and of injury displayed by heart muscle and other excitable tissues. Ann Arbor Univ of Michigan Press, 1933.

Zeft HJ, Cobb FR, Waxman MB, 40. Zeft HJ Cobb FR, Waxman MB, Hunt NC, Morris JJ. Right atrial stimulation in the treatment of atrial flutter. Ann Intern Med. 70:447, 1969.

Zipes DP. The contribution of artificial pacemaking to understanding the pathogenesis of arrhythmias. Am J Cardiol. 28:211, 1971.

Zipes DP, Jackman WM, Heger JJ, et al. Clinical transvenous cardioversion of recurrent life-threatening ventricular tachyarrhythmias: low energy synchronized cardioversion of ventricular tachycardia and termination of ventricular fibrillation in patients using a catheter electrode. Am Heart J. 103:798, 1982.

Zoll PM, Linenthal AJ, Gibson W, Paul MH, Norman LR. Termination of ventricular fibrillation in man by externally applied electric countershock. New Engl J Med. 254:727, 1956.

Zoll PM, Linenthal PJ. Termination of refractory tachycardia by external countershock. Circulation. 25:596, 1962.