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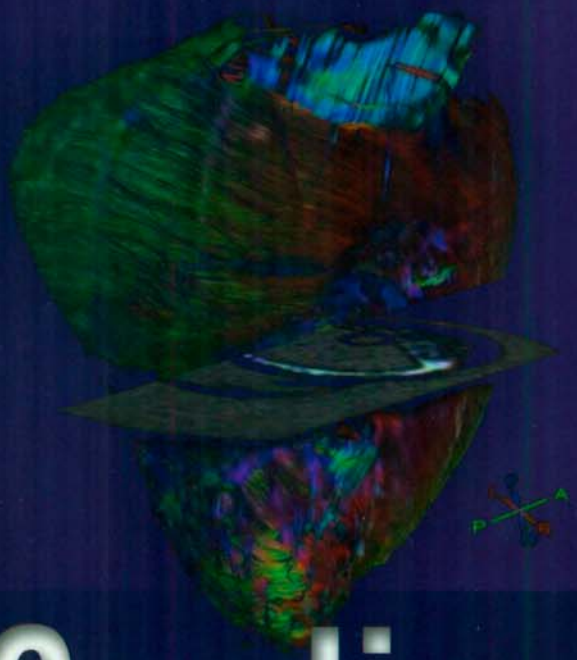
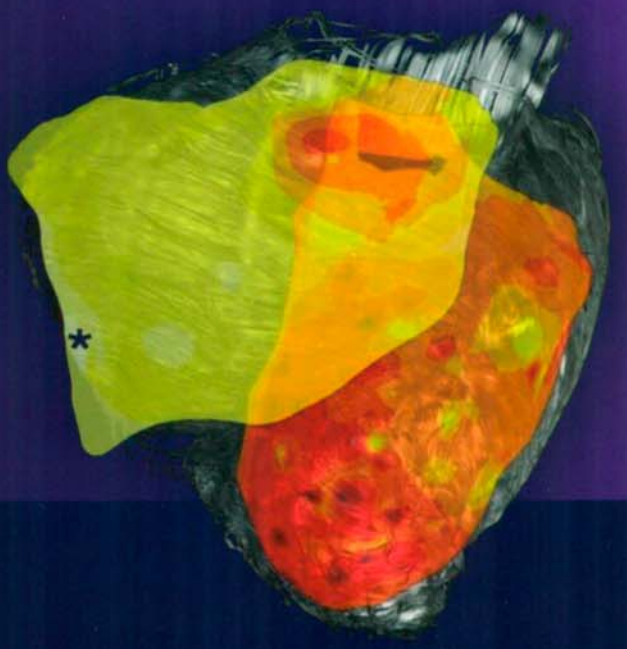
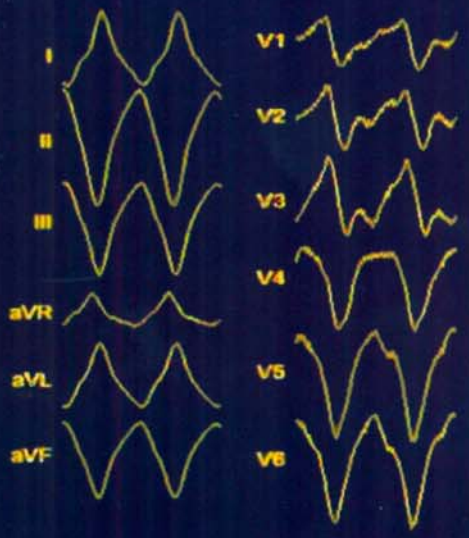
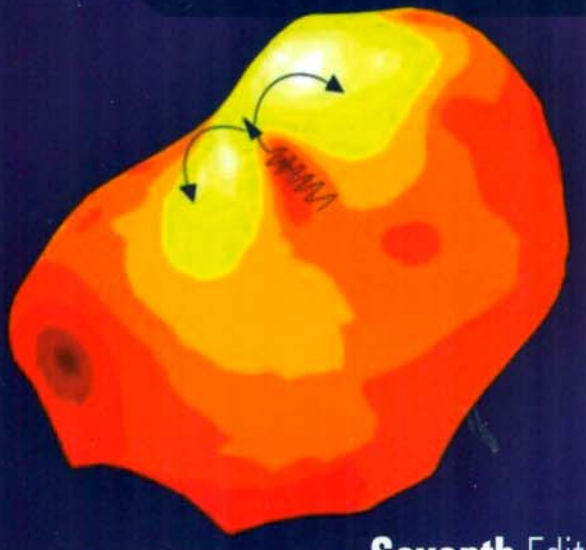




Cardiac Electrophysiology

From Cell to Bedside





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Seventh Edition

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Chapter Outline

Treatment of cardiac arrhythmias using antiarrhythmic drugs (AADs) has two main objectives: relieve symptoms and complications (improve quality of life) and reduce mortality directly related to the arrhythmia.[1] A basic principle in pharmacology is that the best treatment is targeted specifically to disease mechanisms. However, in many patients the ultimate underlying mechanisms of the arrhythmia remain incompletely understood. Thus the choice of a given AAD is empiric and based on the characteristics of the arrhythmia, the pharmacological properties of the AAD, and, above all, its safety profile. Moreover, depending on the underlying structural heart disease (i.e., coronary artery disease [CAD], heart failure [HF], left ventricular [LV] hypertrophy, or hypertension), triggers and arrhythmogenic substrates can vary among patients with the same arrhythmia. This variation could explain why AADs produce widely divergent effects, ranging from termination of the arrhythmia to inefficacy, to exacerbation of the treated arrhythmias, or to generation of entirely new ones (proarrhythmia), in different patients. Unfortunately, the risk of life-threatening proarrhythmia increases with chronic treatment and in patients with structural heart diseases who can benefit more from treatment.

Catheter ablation has emerged as an effective alternative therapy for patients with supraventricular (SVT) and ventricular tachycardias (VT), and the implantable cardioverter defibrillator (ICD) has become standard therapy for patients with life-threatening ventricular arrhythmias. Nevertheless, AAD therapy continues to play a key role in preventing recurrences or reducing their frequency in patients with relatively infrequent episodes of benign tachycardias, with recurrences following catheter ablation procedures, and/or with an ICD to decrease the frequency of shocks as an additional therapy to reduce the number of necessary shocks.

Until recently, arrhythmias were primarily considered to be a purely electrophysiological problem. AADs mainly target cardiac Na^+, Ca^{2+}, and K^+ ion channels (Fig. 54.1). They bind to specific receptor sites within the channel, drug affinity being strongly modulated by the channel state in a time- and voltage-dependent manner. In addition, some AADs modulate the autonomic tone, primarily by antagonizing β1-adrenoceptors (β-blockers) or muscarinic receptors (atropine) or by stimulating adenosine A1 receptors (adenosine) (Table 54.1).

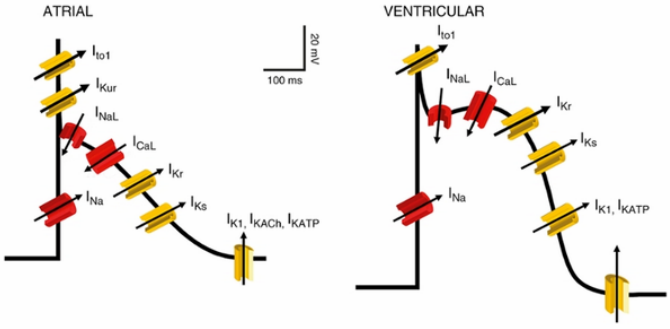

FIGURE 54.1 **Ionic currents involved in shaping of human atrial (*left*) and ventricular…**