

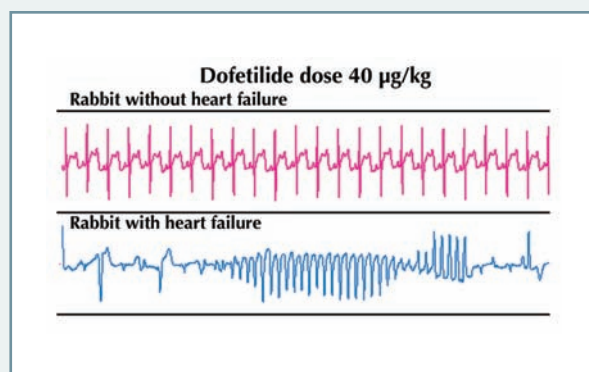
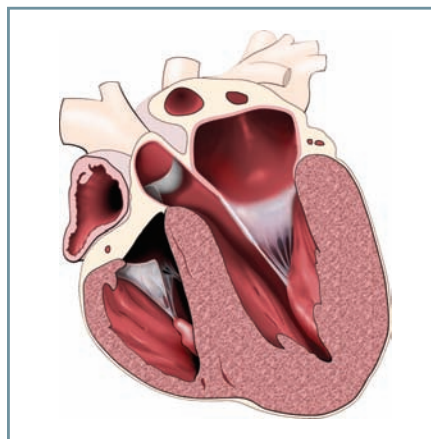
Disease Models

Canine, Rabbit or Guinea Pig Heart

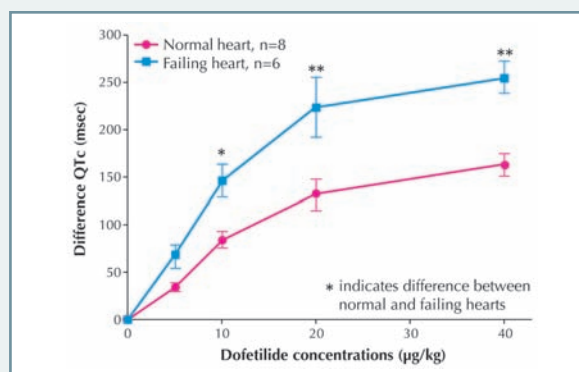
Disease Models - Tests the enhanced potential for drug toxicity frequently associated with disease

- Permissive to torsade de pointes
- More realistic modeling of targeted patient populations
- May be evaluated with conscious and/or Langendorff preparations
- Validated acquisition and analysis systems
- GLP compliant

Toxicity is often exaggerated in states such as left ventricular hypertrophy, heart failure or diabetes. Potential drug toxicity can be sought in these models.

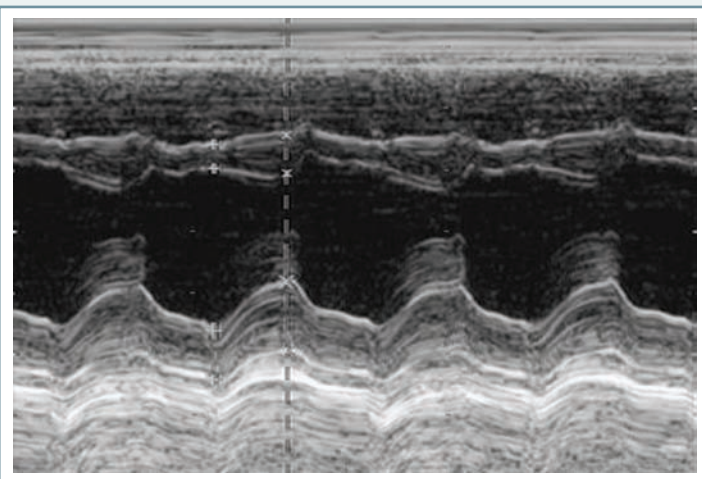


ECGs from normal rabbit (red) and rabbit in heart failure (blue) showing response to dofetilide. Notice that QT is prolonged in the normal rabbit but that torsade de pointes develops in the rabbit with heart failure.

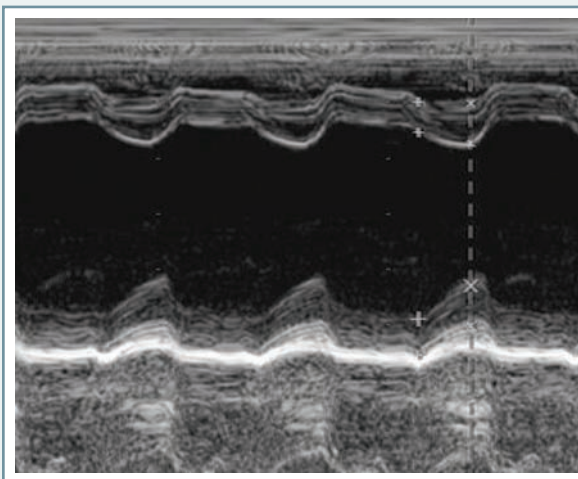


Plot of QTc versus time (dose) after intravenous dosing of dofetilide to conscious rabbits, normal (red) and heart failure (blue). Notice greater prolongation of QTc with heart failure.

Stable heart failure develops within 4 weeks following coronary ligation. Effects of test articles on injury (i.e., infarct size, severity and type of arrhythmia) and on treatment (i.e., inotropic and/or arrhythmic response) may be studied in this model.



M-mode echocardiograms of left ventricular and septal wall motion from rabbit before (left) and after (right) development of heart failure.



Notice increased ventricular volume and decreased fractional shortening - quantitative indicators of the degree of heart failure.



A radiography image of a dog in right lateral recumbency with a pacing lead placed in the right ventricle impacted at the apex for creating a pacing induced heart failure model in dogs.

