

MADIT-RIT: Simple programming change averts most inappropriate ICD therapy

NOV 6, 2012 [Steve Stiles](#)



Los Angeles, CA - A large randomized trial has identified specific programming criteria for implantable cardioverter defibrillator (ICD) devices that, compared with conventional programming, cut the risk of inappropriately delivered therapy by almost 80% [1]. The alternate programming also led to a significant drop in mortality in the patients with primary-prevention ICDs by more than one-half over a follow-up averaging 1.4 years.

The [Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy](#) (MADIT-RIT) supports the use of a fairly easy adjustment to standard ICD programming that could largely alleviate a problem that has long been a weakness of the therapy. Inappropriate treatment of non-life-threatening arrhythmias adds to the distress of patients with the devices and may worsen outcomes.

The study is published online today in the *New England Journal of Medicine*, with lead author **Dr Arthur J Moss** (University of Rochester, NY), to coincide with his presentation of the trial here at the [American Heart Association 2012 Scientific Sessions](#).

ICD survival value underestimated

"The results were striking and a little unexpected," Moss told [heartwire](#). "They first of all showed a reduction in inappropriate therapy due mostly to antitachycardia pacing [ATP], but in addition there was the significant reduction in mortality."

Ordinarily in such patients, ICDs might be counted on to cut the rate of death by about 30%, according to Moss. But with the more successful of the two alternative programming strategies in MADIT-RIT—which initiated device therapy, usually ATP, only with a heart rate of ≥ 200 bpm—"it reduced mortality an additional 55%."

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Allowing patients to tolerate the arrhythmias until the heart rate reached that threshold did not increase the prevalence of fainting spells, contrary to some concerns. But it did seem to help ICDs more frequently avoid delivering therapy to relatively benign supraventricular arrhythmias and some nonsustained ventricular arrhythmias. With conventional programming, ATP tends to kick in at about 170 bpm, Moss observed, but such therapy often isn't needed, because many rhythms in the range of 170 to 200 bpm tend to stop spontaneously without ill effects. And avoiding ATP is a good idea; among other reasons, it's well-known to occasionally induce ventricular fibrillation.



Dr Bruce L Wilkoff

Dr Bruce L Wilkoff (Cleveland Clinic, OH) observed for **heartwire** that MADIT-RIT builds on a rich history of more limited studies like [PREPARE](#), [EMPIRIC](#), and two [PAINFREE](#) trials, as well as [other analyses](#) that explored programming strategies for lowering rates of delivered ICD therapy.

"It would have been very surprising to me if this had not been a positive study, but what we didn't have before was a large, randomized clinical trial," Wilkoff said. "This is a large randomized trial that supports absolutely all the studies that have come before it, with a large and clearly significant outcome. So I think this is huge."

MADIT-RIT, he said, "implies that we've underestimated the survival benefit and overestimated the morbidity of defibrillators."

In his editorial accompanying the trial's publication [2], Wilkoff writes that MADIT-RIT shows "the value of ICD therapy is greatly influenced and in many ways determined by the programming choices made by the physician. A patient's unnecessary exposure to painful shocks and his or her very survival may depend on these choices. Choose wisely!"

"High-rate" vs "delayed" vs conventional therapy



Dr Arthur J Moss

The trial randomized 1500 patients at 98 centers, predominantly in the US but also Canada, Europe, Israel, and Japan. They had either ischemic or nonischemic disease with an indication for a primary-prevention ICD or cardiac-resynchronization therapy device with an ICD (CRT-D), which had to have been their first such device. Patients with atrial fibrillation were excluded.

They were assigned to one of three ICD-programming groups with the primary goal of finding their rate of a first occurrence of inappropriate ATP or shocks: a "high-rate-therapy" group with a 2.5-second delay before starting ATP at a heart rate of >200 bpm; a "delayed-therapy" group with longer delays at different prespecified heart-rate thresholds; and conventional programming with delays of 2.5 seconds for heart rates of 170 to 199 bpm and of 1.0 second for rates ≥ 200 bpm.

Hazard ratio (HR) for a first occurrence of inappropriate therapy and for death in the high-rate^a and delayed-therapy^b groups vs conventional programming^c in MADIT-RIT

End point	High-rate vs conventional programming, HR (95% CI), p	Delayed vs conventional programming, HR (95% CI), p
First occurrence of inappropriate therapy	0.21 (0.13-0.34), <0.001	0.24 (0.15-0.40), <0.001
Death	0.45 (0.24-0.85), 0.01	0.56 (0.30-1.02), 0.06

a. 2.5-second delay before starting ATP at a heart rate of ≥ 200 bpm

b. Rhythm-detection algorithm and a 60-second delay at heart rates of 170 to 199 bpm, a 12-second delay at a rate of 200 to 249 bpm, and a 2.5-second delay at ≥ 250 bpm

c. Delays of 2.5 seconds for heart rates of 170 to 199 bpm and of 1.0 second for rates ≥ 200 bpm

Moss and his colleagues did complete a preliminary analysis of treatment effects by prespecified subgroups according to age, sex, heart-failure etiology and NYHA class, presence of left bundle branch block, QRS duration, and LVEF. "In every single one of them, the hazard ratio stayed below one," Moss said. "There was absolute consistency."

Wilkoff said MADIT-RIT "also tells us a lot about the nature of defibrillator therapy." Generic medications by and large achieve the same therapeutic effects as their proprietary matches, he notes, and ICDs all deliver shocks determined by the same physics regardless of which company makes them. "But, a defibrillator is a different device the moment I program it, and this study shows you how different it is."

MADIT-RIT was funded by Boston Scientific, from which Moss discloses receiving a research grant; disclosures for his coauthors are found at www.nejm.org. Wilkoff discloses board membership with Spectranetics, Medtronic, and St Jude Medical.

Sources

1. Moss AJ, Schuger C, Beck CA, et al. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med* 2012; DOI: 10.1056/NEJMoa1211107. Available at: <http://www.nejm.org>.
2. Wilkoff BL. Improved programming of ICDs. *N Engl J Med* 2012; Available at: <http://www.nejm.org>.

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