Published in final edited form as:
Heart Rhythm. 2009 December 1; 6(12, S1): S41–S45. doi:10.1016/j.hrthm.2009.07.028.

Animal Studies of Epicardial Atrial Ablation

Richard B. Schuessler, PhD, **Anson M. Lee, MD**, **Spencer J. Melby, MD**, **Rochus K. Voeller, MD**, **Sydney L. Gaynor, MBBS**, **Shun-Ichiro Sakamoto, MD**, and **Ralph J. Damiano Jr, MD**
Barnes Jewish Hospital and Washington University in Saint Louis, School of Medicine Division of Cardiothoracic Surgery

Abstract

The Cox-Maze procedure is an effective treatment for atrial fibrillation with a long-term freedom from recurrence of >90%. The original procedure was highly invasive and required cardiopulmonary bypass (CPB). Modifications of the procedure have been proposed so that the procedure can be done without CPB. These approaches proposed to use alternative energy sources, to replace cut and sew lesions with lines of ablation, made from the epicardium on the beating heart. This has been challenging because the atrial wall muscle thickness is extremely variable and can be covered with an epicardial layer of fat. Moreover, the circulating intracavitary blood acts as a potential heat sink, making transmural lesions difficult to obtain. In this report, we summarize the use of nine different unidirectional devices to create continuous transmural lines of ablation from the atrial epicardium in a porcine model. We define a unidirectional device as one in which all the energy is applied by a single transducer on a single heart surface. These include four radiofrequency, two microwave, two lasers, and one cryothermic device. The maximum penetration of any device was 8.3 mm. All devices except one, the Atricure IsolatorT pen, failed to penetrate 2.0 mm in some non-transmural sections. Future development of unidirectional energy sources should be directed at increasing the maximum depth and the consistency of penetration.

Background

Since the introduction of the Cox-Maze procedure (CMP) for the treatment of atrial fibrillation (AF), investigators have sought to make the procedure more accessible to a larger cohort of patients by making the procedure easier to perform and less invasive.(1) The original CMP involved making multiple atrial incisions to create conduction block, preventing reentrant circuits from maintaining atrial fibrillation. However, incising and re-approximating the atria made the CMP technically challenging and required cardiopulmonary bypass. To simplify the procedure, a variety of energy sources have been used to create lesions.(2) These include radiofrequency (RF) (3–5), microwave(6,7), laser(8), high frequency ultrasound(9), and cryothermy (10). To prevent recurrence of AF it is necessary for a device to produce a transmural continuous lesion, because even small gaps in lesions increase the likelihood of recurrence.(11) The most consistently reliable devices for creating transmural lesions have been bipolar RF clamps.(5,12) They can be used to isolate pulmonary veins but cannot be used to create linear lesions on the remainder of the atria without inserting one of the arms of the device into the atrial chambers. In the beating heart, this practice introduces the possibility of air embolism, which in the left atrium, can

Corresponding Author: Richard B. Schuessler, PhD, Division of Cardiothoracic Surgery, 660 South Euclid, Campus Box 8234, Washington University School of Medicine, St. Louis, MO 63110. Phone: 314-362-8300, Fax: 314-361-8706, schuesslerr@wustl.edu.

be catastrophic.(13) Many unidirectional devices have been developed to ablate from the epicardial surface to avoid some of these complications. This report presents a summary of results from nine different unidirectional devices tested in our laboratory to create transmural lesions in the beating heart. (Table 1) The Boston Scientific Flex 4 and Flex 10 and the Medial CV Solar devices are no longer available and have been withdrawn from the market.

Anatomy

It is necessary to delineate human atrial wall thickness to define the performance of any epicardial ablation device. Several studies have examined the regional wall thickness of the right and left atria (LA) of humans. In normal individuals, the atrial thickness in the posterior LA between the pulmonary veins ranged from 2.3±1.0 mm between the superior veins to 2.9±1.3 mm between the inferior veins.(14) In patients with a history of AF, the tissue was thinner, ranging from 2.1±0.9 mm to 2.5±1.3 mm. In both groups, the thickness increased moving from the superior to the inferior veins. In normal individuals, the thickness in the LA just above the coronary sinus was 6.5±2.5 mm. The thickness of Bachmann's bundle, a preferential conduction pathway between the right and left atria crossing across the roof of the atria in the transverse sinus, is 4.6±1.1 mm (range: 1.7–9.3mm) in normal individuals.(15)

In patients with any cardiac disease, the mean LA thickness is 5.2±1.8 (range: 3–15mm). The crista terminalis in the RA has an average thickness of 7.7±2.4 mm (range: 4.2–12.6 mm).(16) These values are only muscle thickness and do not take into account overlying fat or underlying free running pectinate muscles. Even in normal individuals, the fat layer at the posterior mitral annulus can be 10 mm thick.(17) Epicardial fat is a difficult thick barrier to depth of penetration for most ablation technologies. (20) In both the RA and LA, there are also free running pectinate muscles that are not continuous with the epicardial surface. Finally, as patients grow older their chamber size and wall thickness increase.(18) This highly variable wall thickness and anatomy provide a challenge to any unidirectional device to achieve transmural ablation.

Methods

Domestic pigs weighing 70 to 80 kg were used in these studies. All animals received humane care in compliance with the "Guide for the care and use of laboratory animals" published by the National Institutes of Health (publication no. 85-23, revised). Each animal was premedicated with intramuscular ketamine, intubated, and anesthetized with 2% to 4% isoflurane. Heart rate, blood pressure, and oxygen saturation were monitored continuously throughout the procedure. The heart was exposed through a median sternotomy. Lesions were made after systemic heparinization (100 U/kg). Nine different devices were tested including, four RF, two microwave, two lasers, and one cryothermic device. All available energy sources, with the exception of high frequency ultrasound, were tested. All devices were used according to the manufacturer's recommendation. Table 1 summarizes the devices. Multiple lesions were created on each atrium. Following each study, the heart was removed and was visually inspected for intra-atrial thrombus. Each lesion was sectioned at 5mm intervals perpendicular to the long axis of the ablation. Acute sections were stained with 2,3,5-Triphenyltetrazolium chloride (TTC), which was perfused into the heart. Chronic sections were fixed in formalin, molded in paraffin, and stained with Gomori's trichrome stain. Each slide was scanned with a high resolution scanner and evaluated using Adobe Photoshop. The cross sections were examined microscopically to assess tissue thickness and ablation depth. Because some data presented in this report were taken from chronic 30 day studies and others were acute, we tested whether or not TTC accurately predicted the

chronic lesion size. We compared the depth of non-transmural lesions for the Coolrail acutely assessed with TTC to a chronic 30 day study assess by Gomori's Trichrome.

Results

The mean thickness of porcine atria used in this study was 3.7±2.2 mm (range: 0.4mm – 16.1 mm). (Figure 1) The lesion depths were 3.0±1.1 mm for TTC and 3.6±1.5 mm for Trichrome (p=0.15). Thus, it is our opinion that acute histology accurately reflects the chronic lesion depth.

The depth of penetration at different tissue thicknesses for each device is shown in Figures 2 and 3. Points falling on the line of identity were transmural. The results are summarized in Table 2. Only one device, the Atricure Isolator™ Pen, produced completely transmural lesions in each section analyzed. However, the maximum depth of tissue that was examined in this study was only 6.0 mm. All devices, except two, the MedicalCV Solar™ laser and the Flex 10™, penetrated up to 5.5 mm. Alternatively, all devices except one, the Atricure Isolator™ pen, failed to penetrate 2.0 mm in some non-transmural sections. The Surgifrost™ was the only cryothermic device tested. We only assessed whether or not the lesions were or were not transmural. In the region of the pulmonary veins, the superior vena cava, and inferior vena cava the lesions were all transmural. However, over the LA and RA free walls it was only transmural 82% and 79% of the time. Over the coronary sinus it was only transmural 19% of the time.

Discussion

To ablate AF in the beating heart without cardiopulmonary bypass using an epicardial approach, it is essential to create reliable, continuous transmural lesions. The epicardial approach is challenging with atrial thickness varying from less than 1 mm to 17 mm. In addition, in the beating heart there is a continuous flow of blood in the atrial cavity and muscle. This acts as a thermal sink, cooling tissue that is ablated with technologies like RF that heat tissue, and heating tissue that is ablated with cryothermic energy. Another challenge is epicardial fat, which has an electrical conductivity that is 30 times less than muscle.(19) The thermal conductivity is one-third that of muscle. The result is that fat acts as a thermal and electrical insulator reducing the depth of penetration of both heating and cooling technology. For RF energy, even a 2 mm layer of fat significantly reduces the ability to create a transmural lesion.(20) In the normal human, atrial fat layers at the mitral annulus can be as thick as 10 mm. Complex atrial anatomy also confounds epicardial ablation, with free running pectinate muscles present in both the left and right atria. The intervening blood flowing between the epicardial surface and the pectinate muscle prevent ablation of the underlying pectinate muscle.

In the studies presented in this report, the domestic pig was used as a model of the human atria. The thickness of tissue is similar to that in humans, which allows for reliable testing of ablation devices. However, the diseased human atria may have a wall thickness that is greater than that observed in the pig. Furthermore, although there is epicardial fat present on the pig atria, human atria can have significantly more and thicker regions of fat overlaying the muscle.

Only one device, the Atricure Isolator™ RF Pen, produced completely transmural lesions in all sections tested. However, the maximum tissue thickness tested was only 6 mm. The Atricure Coolrail™, which used similar bipolar technology as the isolator pen, only created transmural lesions 77% of the time. Even though there was thicker atrial tissue in that study, it still made non-transmural lesions tissue less than 2 mm thick. The Isolator™ has shorter

electrodes and the ablation time was 15 seconds compared to the Coolrail™ (40–50 seconds). One explanation for this may be that the Coolrail™ may be more difficult to hold in place on the beating atria. However, both the Visitrax™ and Adhere™ devices use suction to keep them in place and both also failed to produce reliable transmural lesions. The Visitrax™ and Adhere™ both made non-transmural lesions in tissue less than 2 mm thick. All these RF devices can produce lesions that are >5mm, so it is not clear why all but one (Isolator™ Pen) fails to penetrate 2 mm under some conditions.

Two microwave devices, the Flex 4™ and Flex 10™ failed to make continuous transmural lesions reliably. The Flex 4™ and Flex 10™ are 4 cm and 10 cm long respectively. It was more difficult to maintain contact along the whole length of the devices. The microwave device active electrode is directional, so it was difficult at times to maintain contact, and to keep the active surface directed toward the epicardium particularly in areas of high curvature.

Two different laser systems were tested, the Edwards Optiwave™ and the MedicalCV Solar™. In addition to the need to maintain contact, like microwave the devices are directional. Both devices had a low efficacy for making transmural lesions. The Solar™ used suction to maintain contact and keep the laser pointed at the epicardial surface. Despite this, it was only able to penetrate a maximum of 3.3 mm, which accounted for the low percent of sections that were transmural.

Only one cryosurgical device was tested, the ATS (formerly Cryocath) Surgifrost™ device. In these studies, tissue thickness or depth of penetration was not measured. The only endpoint of this study was lesion transmurality. The failure to make transmural lesions over the coronary sinus is consistent with the greater wall thickness and presence of fat in this region. Failures in the RA and LA free walls may be a result of the free running pectinate muscles.

There are a number of limitations in summarizing multiple studies on different devices. First, the devices were not randomized. Second, different lesion sets were used for different devices, resulting in different thicknesses of ablated target tissue. Finally, different numbers of animals were studied with each device. Studies of others have also obtained different results when using some of these devices.(4) It should also be noted that manufacturers are continuing to update devices and generators addressing issues raised in these studies. However, this report does show some of the limitations of the use of epicardial devices. Moreover, all studies were done in the same laboratory, under similar experimental conditions, and under the guidance of the two senior authors (RBS, RJD).

In summary, although the devices tested have demonstrated the ability to penetrate through the atrial wall under certain circumstances, in practice they do not always penetrate nearly as far as the maximum possible depth for that device. The reason for this failure is likely multifactorial and device-dependent. Clearly, the biophysical characteristics of the device and its particular ablation technology play an extremely important role. The percent of transmural lesions varied for a minimum of 5% up to 100% for the different devices tested in our laboratory (Tables 1 and 2). Another challenge is the heterogeneity of atrial anatomy. In our porcine model, atrial wall thickness varied for a minimum of 0.4 mm to a maximum of 16 mm. At its thickest dimensions, none of the devices tested demonstrated the ability to penetrate that deep. Use of these devices for epicardial ablation will require knowledge of the wall thickness of atria. In the region around the pulmonary veins, lesion transmurality should be possible due to relatively thin tissue in this area. However, reliable transmurality may be difficult over Bachmann’s Bundle, the crista terminalis and at the mitral or tricuspid annuli with any device due to the thickness of the tissue.

Acknowledgments

This study was supported by Grants NIH R01 HL 032257, NIH R01 HL085113 and NIH T32 HL007776. Devices and funding were provided by Atricure, Inc, Boston Scientific, Cryocath Technologies, Edwards Lifesciences, Estech, MedicalCV, Inc, and nContact Surgical, Inc.

References

1. Cox JL, Schuessler RB, D'Agostino HJ Jr, Stone CM, Chang BC, Cain ME, et al. The surgical treatment of atrial fibrillation. III. Development of a definitive surgical procedure.[see comment]. Journal of Thoracic & Cardiovascular Surgery. 1991; 101(4):569–83. [PubMed: 2008095]
2. Lall SC, Damiano RJ Jr. Surgical ablation devices for atrial fibrillation. J Interv Card Electrophysiol. 2007 Dec; 20(3):73–82. [PubMed: 18175210]
3. Sakamoto S, Voeller RK, Melby SJ, Lall SC, Chang NL, Schuessler RB, et al. Surgical ablation for atrial fibrillation: the efficacy of a novel bipolar pen device in the cardioplegically arrested and beating heart. J Thorac Cardiovasc Surg. 2008 Nov; 136(5):1295–301. [PubMed: 19026819]
4. Kiser AC, Nifong LW, Raman J, Kasirajan V, Campbell N, Chitwood WR Jr. Evaluation of a novel epicardial atrial fibrillation treatment system. Ann Thorac Surg. 2008 Jan; 85(1):300–3. [PubMed: 18154827]
5. Prasad SM, Maniar HS, Schuessler RB, Damiano RJ Jr. Chronic transmural atrial ablation by using bipolar radiofrequency energy on the beating heart. Journal of Thoracic & Cardiovascular Surgery. 2002; 124(4):708–13. [PubMed: 12324728]
6. Gaynor SL, Byrd GD, Diodato MD, Ishii Y, Lee AM, Prasad SM, et al. Microwave ablation for atrial fibrillation: dose-response curves in the cardioplegia-arrested and beating heart. Ann Thorac Surg. 2006 Jan; 81(1):72–6. [PubMed: 16368338]
7. Melby SJ, Zierer A, Kaiser SP, Schuessler RB, Damiano RJ Jr. Epicardial microwave ablation on the beating heart for atrial fibrillation: the dependency of lesion depth on cardiac output.[see comment]. Journal of Thoracic & Cardiovascular Surgery. 2006; 132(2):355–60. [PubMed: 16872962]
8. Williams MR, Casher JM, Russo MJ, Hong KN, Argenziano M, Oz MC. Laser energy source in surgical atrial fibrillation ablation: preclinical experience. Ann Thorac Surg. 2006 Dec; 82(6):2260–4. [PubMed: 17126144]
9. Mitnovetski S, Almeida AA, Goldstein J, Pick AW, Smith JA. Epicardial high-intensity focused ultrasound cardiac ablation for surgical treatment of atrial fibrillation. Heart Lung Circ. 2009 Feb; 18(1):28–31. [PubMed: 19084476]
10. Gaita F, Riccardi R, Caponi D, Shah D, Garberoglio L, Vivalda L, et al. Linear cryoablation of the left atrium versus pulmonary vein cryoisolation in patients with permanent atrial fibrillation and valvular heart disease: correlation of electroanatomic mapping and long-term clinical results. Circulation. 2005; 111(2):136–42. [PubMed: 15623545]
11. Melby SJ, Lee AM, Zierer A, Kaiser SP, Livhits MJ, Boineau JP, et al. Atrial fibrillation propagates through gaps in ablation lines: implications for ablative treatment of atrial fibrillation. Heart Rhythm. 2008 Sep; 5(9):1296–301. [PubMed: 18774106]
12. Melby SJ, Gaynor SL, Lubahn JG, Lee AM, Rahgozar P, Caruthers SD, et al. Efficacy and safety of right and left atrial ablations on the beating heart with irrigated bipolar radiofrequency energy: a long-term animal study. Journal of Thoracic & Cardiovascular Surgery. 2006; 132(4):853–60. [PubMed: 17000297]
13. Doll N, Borger MA, Fabricius A, Stephan S, Gummert J, Mohr FW, et al. Esophageal perforation during left atrial radiofrequency ablation: Is the risk too high? J Thorac Cardiovasc Surg. 2003 Apr; 125(4):836–42. [PubMed: 12698146]
14. Platonov PG, Ivanov V, Ho SY, Mitrofanova L. Left atrial posterior wall thickness in patients with and without atrial fibrillation: data from 298 consecutive autopsies. J Cardiovasc Electrophysiol. 2008 Jul; 19(7):689–92. [PubMed: 18284501]
15. Saremi F, Channual S, Krishnan S, Gurudevan SV, Narula J, Abolhoda A. Bachmann Bundle and its arterial supply: imaging with multidetector CT--implications for interatrial conduction abnormalities and arrhythmias. Radiology. 2008 Aug; 248(2):447–57. [PubMed: 18641248]

16. Ren JF, Marchlinski FE, Callans DJ, Zado ES. Echocardiographic lesion characteristics associated with successful ablation of inappropriate sinus tachycardia. J Cardiovasc Electrophysiol. 2001 Jul; 12(7):814–8. [PubMed: 11469434]

17. Cabrera JA, Ho SY, Climent V, Sanchez-Quintana D. The architecture of the left lateral atrial wall: a particular anatomic region with implications for ablation of atrial fibrillation. Eur Heart J. 2008 Feb; 29(3):356–62. [PubMed: 18245120]

18. Pan NH, Tsao HM, Chang NC, Chen YJ, Chen SA. Aging dilates atrium and pulmonary veins: implications for the genesis of atrial fibrillation. Chest. 2008 Jan; 133(1):190–6. [PubMed: 18187745]

19. Berjano EJ, Hornero F. Thermal-electrical modeling for epicardial atrial radiofrequency ablation. IEEE Trans Biomed Eng. 2004 Aug; 51(8):1348–57. [PubMed: 15311819]

20. Hong KN, Russo MJ, Liberman EA, Trzebucki A, Oz MC, Argenziano M, et al. Effect of epicardial fat on ablation performance: a three-energy source comparison. J Card Surg. 2007 Nov–Dec; 22(6):521–4. [PubMed: 18039220]

Figure 1 A

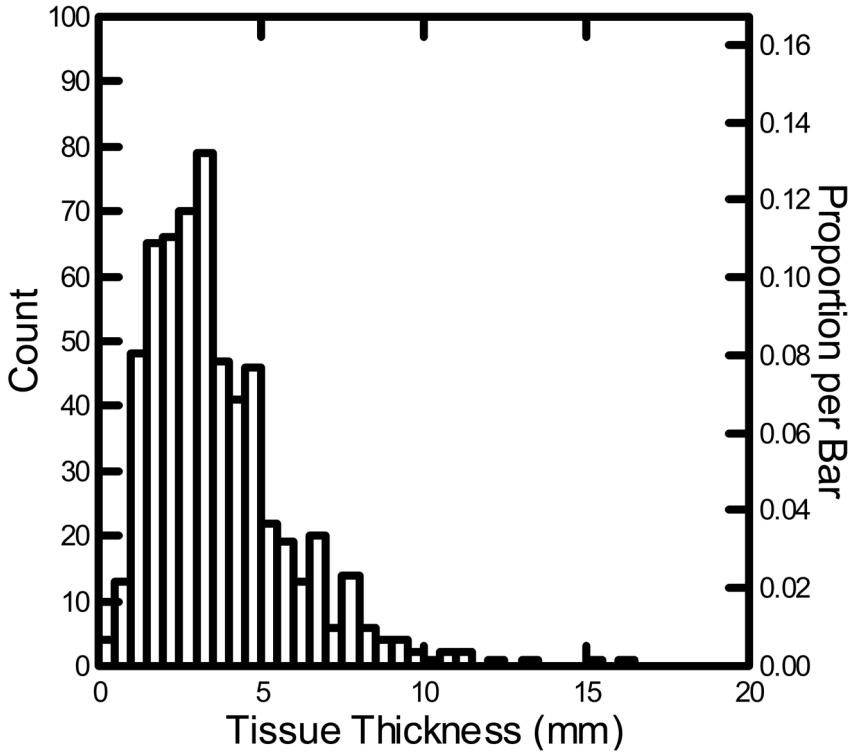

Figure 1 B

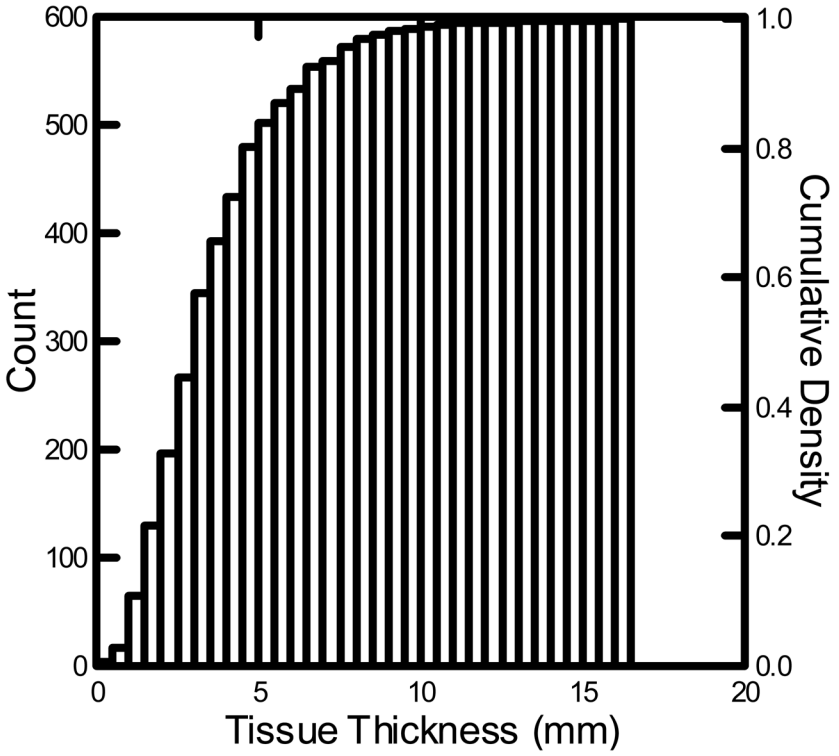

Figure 1.
Histogram of the distribution of atrial tissue thickness in the pig (left panel). Cumulative histogram of tissue thickness (right panel).

Figure 2 A

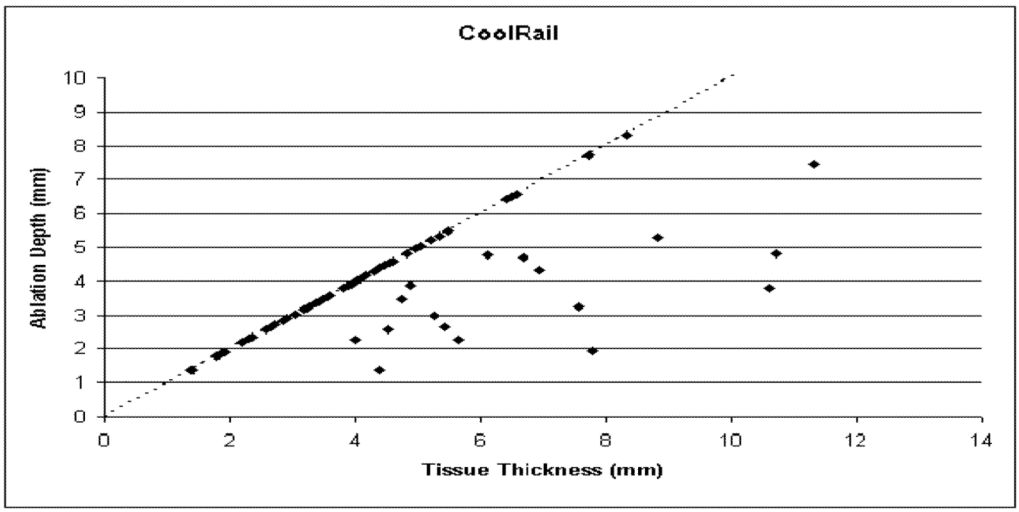

Figure 2 B

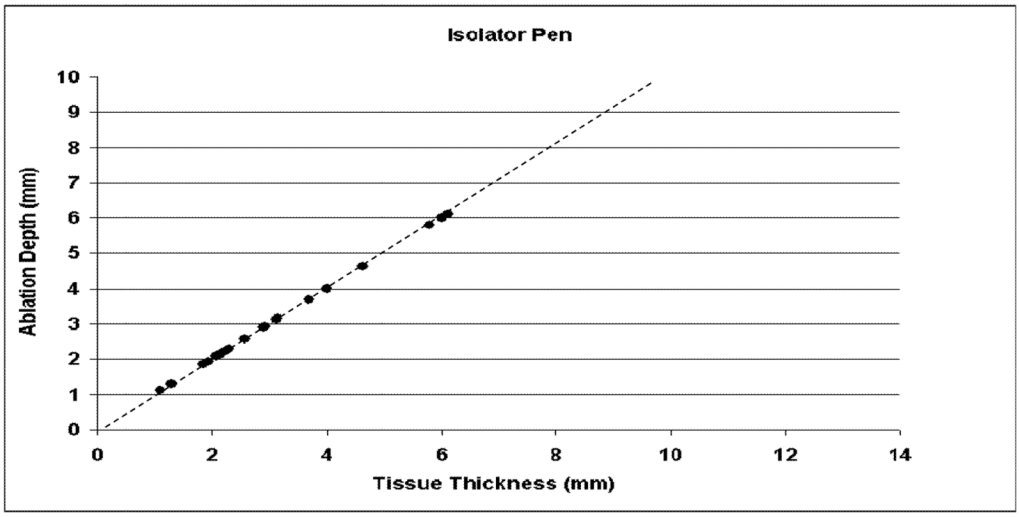

Figure 2 C

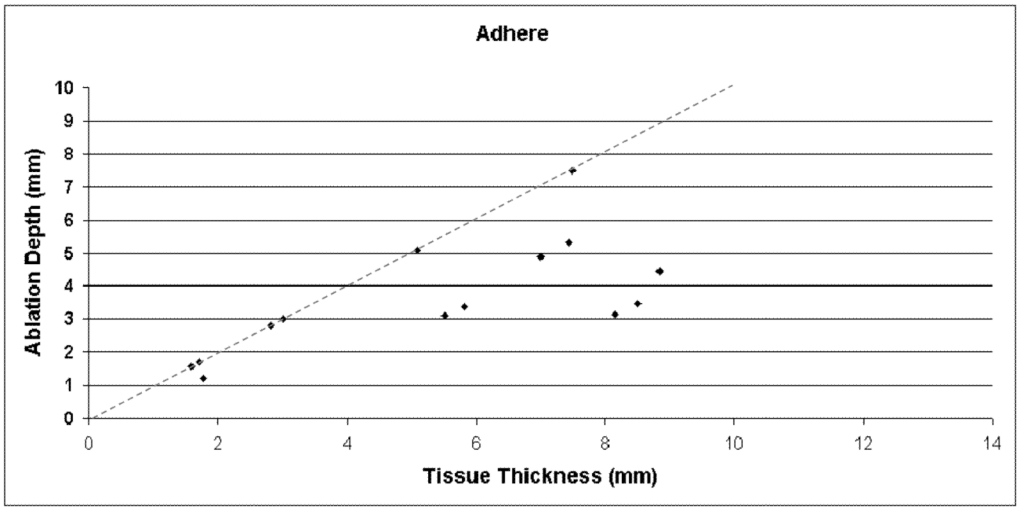

Figure 2 D

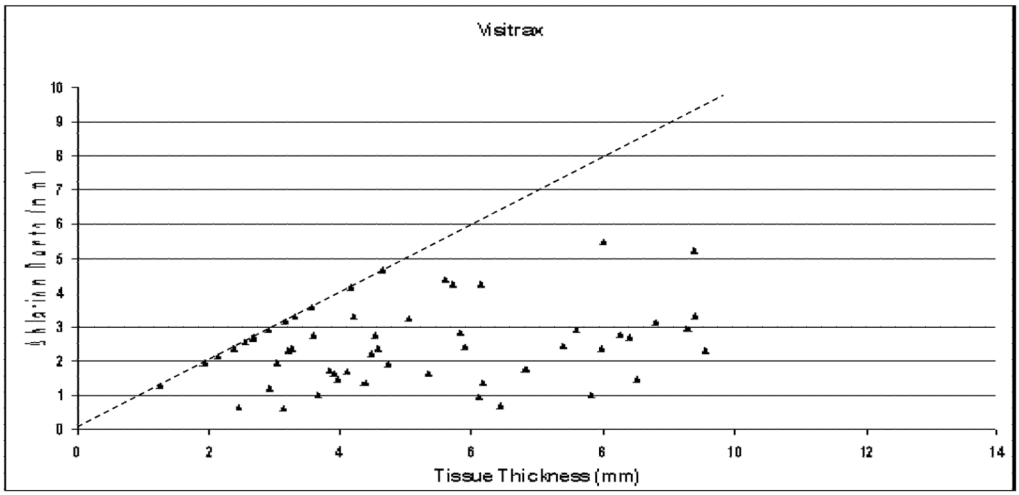

Figure 2.

Scatter plots of tissue thickness versus ablation depth for four RF devices. The line of identity represents transmural ablation. Any point below the line is not transmural. The upper left panel is the Coolrail™ device and the upper right panel is the Isolator™ Pen. The lower left panel is the Adhere™ device and the lower right is the Visitrax™ device.

Figure 3A

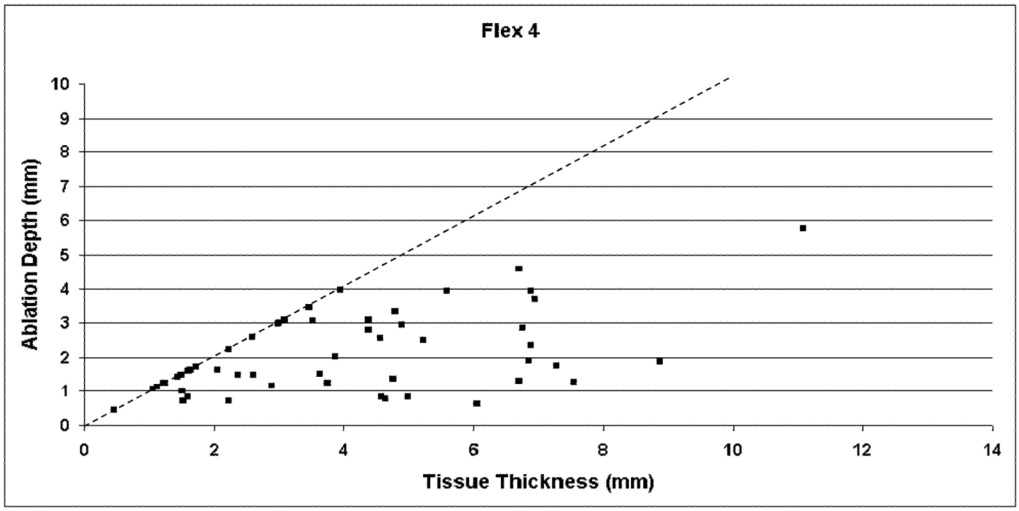

Figure 3B

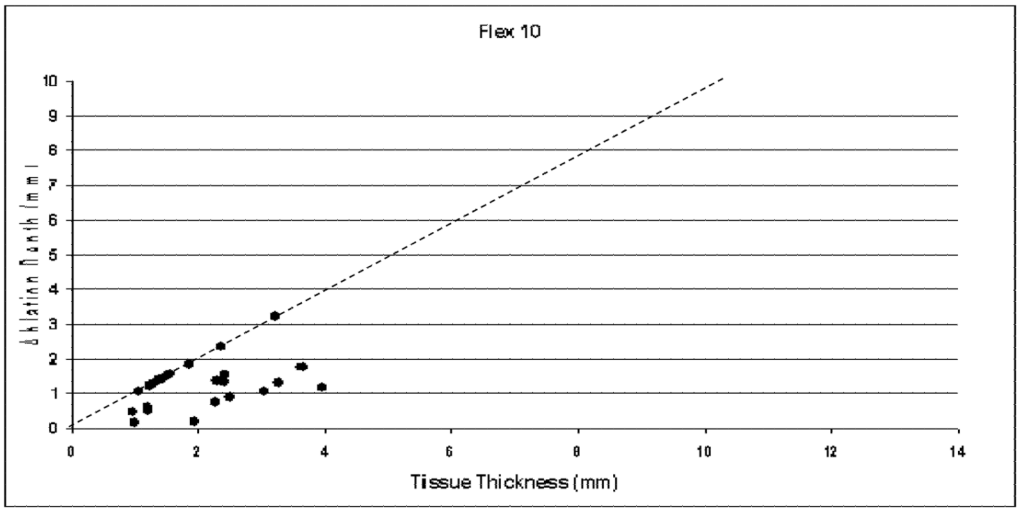

Figure 3 C

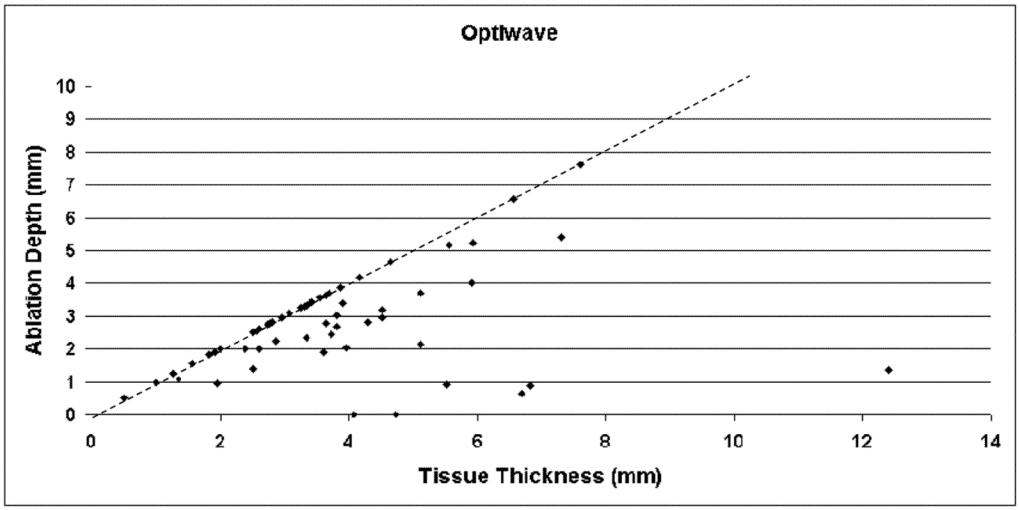

Figure 3 D

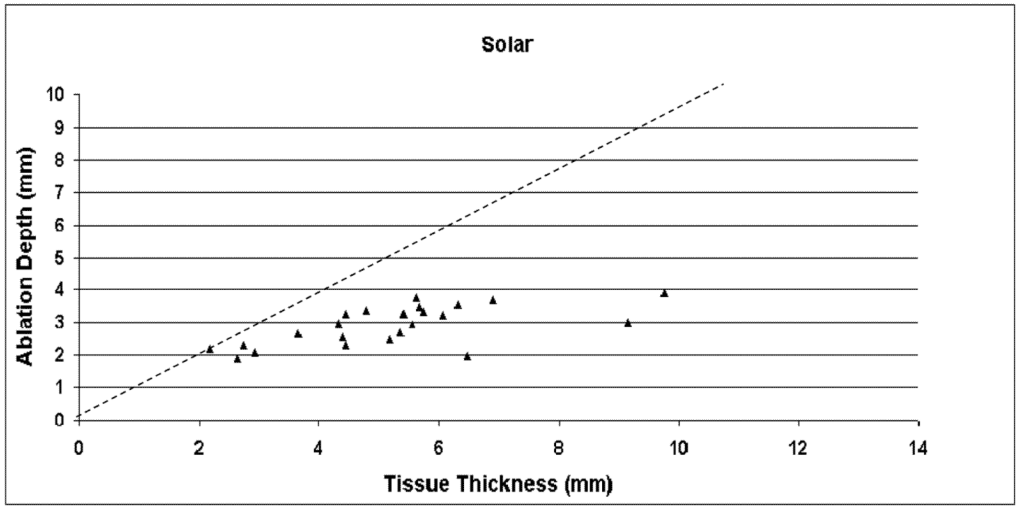

Figure 3.
Scatter plots of two microwave devices, the Flex 4™ (upper left) and Flex 10™ (upper right). The lower two panels are two lasers, the Optimax™ (lower left) and the Solar™ (lower right).

Table 1

Summary of Devices. The trade name of the device, manufacturer, energy source, recommended application time, and whether or not it was an acute or chronic study are shown. The Boston Scientific Flex 4 and Flex 10 and the Medial CV Solar devices are no longer available.

Device	Manufacturer	Energy	Ablation Time	Acute/Chronic
CoolRail™	AtriCure	RF	40–50 sec	Chronic
Isolator Pen™	AtriCure	RF	15 sec	Acute
Visitrax™	nContact Surgical	RF	120 sec	Acute
Cobra Adhere™	Estech	RF	120 sec	Acute
Flex 4™	Boston Scientific	Microwave	90 sec	Acute
Flex 10™	Boston Scientific	Microwave	90 sec	Acute
Optiwave™	Edwards Lifesciences	Laser	120 sec	Acute
Solar™	MedicalCV	Laser	80–100 sec	Acute
Surgifrost™	Cryocath Technologies	Cryothermic	120 sec	Chronic

Table 2

Summary of Device Performance. The percent of sections examined that were transmural, the maximum tissue thickness of the sections examined, the maximum depth of penetration in any section, and the minimum depth of penetration of any section that was not transmural.

Device	% Transmural	Max Tissue Thickness (mm)	Max Penetration (mm)	Min Penetration (mm)
CoolRail™	77.0	11.3	8.3	1.4
Isolator Pen™	100.0	6.0	6.0	6.0
Visitrax™	15.0	9.3	5.5	0.6
Cobra Adhere™	40.0	8.8	7.5	1.2
Flex 4™	40.0	11.1	5.8	0.8
Flex 10™	46.0	4.0	3.2	0.2
Optiwave™	55.0	16.0	7.6	0.0
Solar™	5.0	5.4	3.3	1.9
Surgifrost™	70.0	-	-	-