Comparison of longevity and clinical outcomes of implantable cardioverter-defibrillator leads among manufactures

Short title: Longevity and clinical outcomes of ICD leads

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First author's surname: Kawada

Satoshi Kawada[a], MD, Nobuhiro Nishii[b], MD, PhD, Yoshimasa Morimoto[a], MD, Akihito Miyoshi[a], MD, Motomi Tachibana[a], MD, Hiroyasu Sugiyama[a], MD, Koji Nakagawa[a], MD, PhD, Atsuyuki Watanabe[a], MD, PhD, Hiroshi Morita[b], MD, PhD and Hiroshi Ito[a], MD, PhD.

[a]*Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.*

[b]*Department of Cardiovascular Therapeutics, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.*

Correspondence to: Satoshi Kawada, MD, Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan

Tel: +81-86-235-7351; Fax: +81-86-235-7353

E-mail: satoshikawada03@gmail.com, satoshikawada3@yahoo.co.jp

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ABSTRACT

Background: An early failure of the Biotronik Linox S/SD implantable cardioverter defibrillator (ICD) lead has been reported. We have also experienced several cases with early failure of Linox leads.

Objective: Our aim was to assess the longevity of Linox S/SD (Biotronik, Berlin, Germany) compared to Sprint Fidelis (Medtronic, Minneapolis, MN), Sprint Quattro (Medtronic) and Endotak Reliance (Boston Scientific, Natick, Masachusetts) leads.

Methods: We retrospectively reviewed patients who had undergone implantation of Linox S/SD (n=90), Sprint Fidelis (n=37), Sprint Quattro (n=27) or Endotak Reliance (n=50) leads between June 2000 and December 2013 at our hospital. Variables associated with lead failure were assessed by the Kaplan-Meier method and Cox survival modeling.

Results: Failure rates of Linox, Sprint Fidelis, and Endotak leads were 3.2%/year (7-year survival rate, 81.0%), 3.4%/year (7-year survival rate, 77.2%), and 0.61%/year (7-year survival rate, 95.8%), respectively. No lead failure was found with Sprint Quattro leads. The survival probability of Linox leads was significantly lower than that of Endotak leads (P=0.049), and comparable to that of Sprint Fidelis leads (P=0.69). In univariate analysis, age was the only predictor of Linox lead failure. Patients <58 years

old were at significantly increased risk of lead failure compared with patients ≥58 years old (hazard ratio, 9.0; 95% confidence interval, 1.13-71.3; P=0.037).

Conclusion: In our single-center experience, the survival rate of Linox leads was unacceptably low. The only predictor of Linox lead failure was age at implantation. This is the first description of a lower survival rate for Linox leads in an Asian population.

Keywords: implantable cardioverter-defibrillator; longevity of ICD lead; Linox; Sprint Fidelis; Sprint Quattro; Endotak Reliance

INTRODUCTION

Implantable cardioverter-defibrillators (ICDs) prevent sudden cardiac death (SCD) and improve clinical outcomes in patients for either primary or secondary prevention of SCD.[1-2] Despite their proven efficacy and relative safety, several complications associated with defibrillators and transvenous leads have been reported. Lead dysfunction is a major concern in ICD recipients, whether due to manufacturing defects or random failure. An increased rate of lead fracture as compared to other manufacturers could result in a product being withdrawn from the market. In 2007, The Sprint Fidelis leads (Medtronic, Minneapolis, MN) were reported to show an increased rate of fracture.[3] This lead had been withdrawn from the market in October 2007 because it was prone to fracture, resulting in inappropriate or inefficient shocks, or failure to pace. The fracture rate reportedly approaches 17% at 5 years.[3] In 2011, St Jude Medical (Sylmar, CA) issued a medical advisory regarding increased externalized conductors of Riata/Riata ST leads.[4] These advisories were upgraded to FDA class Ⅰ recalls in October 2007 and December 2010, respectively.

Linox S (single coil) leads and SD (dual coil) leads (Biotronik, Berlin, Germany), as 7.8-Fr silicone-insulated ICD leads, were released in 2006 and 2007, respectively. More than 85,000 of these leads had been implanted worldwide as of 2016.[5] Although product

performance reports by Biotronik have indicated cumulative lead survival of 95.2% at 7 years for the Linox S and 95.0% at 9 years for the Linox SD, almost all reports from Europe and North America have suggested unacceptably high rates of lead failure, contradicting the self-reported data from the manufacturer.[6,7] We have also encountered several cases of early Linox ICD lead failures in our hospital. However, the performance of Linox leads and clinical outcomes in Asian populations have not been clarified. We therefore examined the longevity and clinical outcomes of Linox leads at our hospital. Results from these analyses were compared with data for Sprint Fidelis (model 6949), Sprint Quattro (models 6935, 6944 and 6947) and Endotak Reliance leads (Boston Scientific, Natick, Massachusetts) (models 0174, 0175, 0185, 0292 and 295) implanted at Okayama University Hospital.

METHODS

Subjects

We conducted a retrospective review of patients with Linox S/SD leads, Sprint Fidelis leads (Medtronic, model 6949), Sprint Quattro leads (Medtronic, model 6935, 6944 and 6947) and Endotak Reliance leads (Boston Scientific, model 0174, 0175, 0185, 0292 and 295) implanted between June 2000 and December 2013 at our hospital.

Demographic and clinical records of all patients were obtained from our hospital records and device database, including patient characteristics, cardiovascular history, and various parameters of ICD leads. All study protocols were approved by the institutional review board at Okayama University Hospital.

ICD lead implantation

ICD leads were implanted via a left- or right-sided cephalic vein by cut-down or, alternatively, from the subclavian vein using standard puncture or introducer sheath techniques, mainly under local anesthesia, or sometimes under general anesthesia. ICD leads were positioned in the myocardium around the right ventricular apex. After ICD lead implantation, pacing threshold, R-wave amplitude and lead impedance were measured in all patients, and defibrillation threshold testing was performed. All patients were evaluated in the outpatient clinic at 1 month after implantation. Patients were then seen every 3-6 months with in-clinic device interrogation or by remote monitoring (RM) when informed consent was obtained from the subject.

Definition of lead failure

Lead failure was defined as one of the following: 1) recurrent non-physiological high rate sensing (electrical noise); 2) a sudden pace/sense or high-voltage impedance change (>100% increase or >50% decrease) or values outside the interval of 200-1500 Ω or 20-200 Ω, respectively; 3) a sudden or intermittent increase in right ventricular threshold and/or decrease in R-wave amplitude, without alternative explanation. Lead dislodgements, physiological oversensing, and T-wave oversensing without lead electrical dysfunction were not considered as lead failures for the purposes of this study.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation or median and interquartile range (IQR) and were compared between groups using Student's t-test. Categorical variables are expressed as numbers and proportions and were compared using the chi-squared test. For each variable that was significantly associated with the occurrence of lead failure, a hazard ratio with 95% confidence interval (CI) was calculated using Cox proportional analysis. Survival and cumulative hazards were calculated using the Kaplan-Meier Method. Differences between survival curves were compared using the log rank test. All statistical analyses were performed using SPSS

version 24.0 software (SPSS, Chicago, IL). Values of $P<0.05$ were considered statistically significant.

RESULTS

Baseline patient characteristics

A total of 204 patients (Linox, n=90; Sprint Fidelis, n=37; Sprint Quattro, n=27; and Endotak Reliance, n=50) received implantation of an ICD or cardiac resynchronization therapy with defibrillator (CRT-D) in our hospital between June 2000 and December 2013. Baseline characteristics of the participants in this study are shown in Table 1.

Significant differences in some baseline characteristics were identified in our study population. The median interval from implantation to last follow-up was significantly shorter for Sprint Quattro leads than for other leads. Among the baseline characteristics examined in this study, proportion of female gender and the mean total number of leads implanted, prevalence of CRT, dual coil, and passive lead fixation differed significantly between groups. Concentration of brain natriuretic peptide (BNP) and left ventricular ejection fraction (LVEF) also differed between groups.

Clinical outcomes

During follow-up, we identified lead failure in 10 Linox leads (11.1%), 8 Sprint Fidelis leads (21.6%), and 1 Endotak Reliance lead (2%). Median times from implantation to lead failure for the Linox, Sprint Fidelis leads after implantation were 55.8 months (IQR, 29.4-60.1 months) and 62.3 months (IQR, 44.0-72.5 months), respectively (P=0.343) (1 Endotak Reliance lead failure occurred 82.9 months after implantation). Seven-year lead survival rates were 81.0%, 77.2%, and 95.8% for Linox, Sprint Fidelis, and Endotak Reliance, respectively. No lead failure was found in the Sprint Quattro lead cohort. Figure 1 shows the Kaplan-Meier curves of cumulative survival rates for Linox, Sprint Fidelis, Sprint Quattro, and Endotak Reliance groups. Significant differences were seen between all 4 groups (P=0.021). The probability of lead survival was significantly decreased in Linox and Sprint Fidelis leads as compared with Endotak Reliance leads according to the log-rank test (P=0.049, P=0.023, respectively). No significant difference in lead survival probability was evident between Linox and Sprint Fidelis leads (P=0.69). Failure rates for Linox, Sprint Fidelis, and Endotak Reliance were 3.2%/year, 3.4%/year, and 0.61%/year, respectively.

Clinical features of Linox lead failure

The clinical features and device data for Linox lead failure are given in Table 2. In 7 leads, pace/sense impedance rose (>1500 Ω) with conductor abnormality and in two leads, pace/sense or high-voltage impedance decreased (<200 Ω or <20 Ω) with insulation failure. One case showed increased pacing threshold without any lead abnormalities. Although 5 of the 10 cases displayed non-physiological high rate sensing episodes, only one patient suffered from inappropriate ICD shock. In Patient 8, lead impedance had gradually increased to more than 2500 Ω for 1 month, followed by notification of a device alert on RM without any ICD therapy or pacing failure (Figure 2). Lead extraction was successfully performed in two patients (Patients 4 and 9). The two extracted leads were submitted to the manufacturer for additional testing. In the lead of Patient 4, abrasion of the external insulation with conductor exposure caused by lead-to-can interaction in the prepectoral pocket was recognized (Figure 3A). In the lead of Patient 9, significant insulation abrasion within the ICD pocket was recognized, but without conductor exposure. New ICD leads were added in all patients without any complications.

Predictors of Linox lead failure

Table 3 shows univariate analysis of baseline characteristics and electrical parameters for Linox leads. Univariate analysis was applied to evaluating associations of potential predictive factors to Linox lead failure. We divided our population into two age groups according to the median age of 58 years. Linox leads implanted in patients <58 years old showed significantly lower survival probability than those in patients ≥58 years old (P=0.01) (Figure 4). Forty-five Linox TD (dual coil, passive fixation) leads and 45 Linox SD (dual coil, active fixation) leads were implanted in our institute, resulting in 8 lead failures and 2 lead failures, respectively. No significant difference in lead survival rate was seen between Linox TD leads and Linox SD leads (P=0.082). None of gender, body mass index (BMI), venous access method, total number of implanted leads or LVEF influenced lead performance.

We also used Cox proportional hazards regression to examine predictors of lead failure for entire group, but we couldn't identify the significant independent predictor of lead failure. Linox ICDs had a much higher proportion of patients with passive lead, and passive lead was associated with a close to 4 fold increase in risk of ICD failure. We then took into account the difference between active and passive leads and conduct an additional analysis, but we couldn't identify the independent predictor of lead failure.

Adverse events

Only one patient (Patient 7) with Linox lead failure suffered from inappropriate ICD shock. This patient was monitored by a RM system that required use of a wand over the device, and thus could not automatically download and transmit an emergency alert. In this study, three cases of lead failure were detected at routine in-office device follow-ups and 7 cases were detected by wireless RM. RM allowed early and reliable detection of ICD lead failures, and may have prevented the development of inappropriate therapy. In Patient 4, we noticed an emergency alert for VF detection on RM. However, the cause of the alert was not true VF, but instead non-physiological high rate sensing (Figure 3B). Fortunately, ICD therapy was avoided because of early notification and admission for the event. The interrogation disclosed the presence of a lead fracture (sudden right ventricular impedance rise to >1500 Ω). No patients experienced serious injury as a result of lead failure.

DISCUSSION

Main findings

Our study had three main findings. First, failure rates for the Linox, Sprint Fidelis, and Endotak Reliance were 3.2%/year, 3.4%/year, and 0.61%/year, respectively. No lead

failure was found in the cohort with Sprint Quattro leads. Overall Linox lead survival at 7 years in our single-center experience was 81%, resulting in poor outcome comparable to those of Sprint Fidelis leads (7-year survival, 77.2%; P=0.69). Second, this represents the first description of a lower survival probability for Linox leads in Asian populations. Third, in univariate analysis, patients <58 years old were at significantly increased risk of lead failure compared with patients ≥58 years old (hazard ratio, 9.0; 95% confidence interval, 1.13-71.3; P=0.037).

Inherently, lead failure is a function of three factors, patient factors (including size of the patients, ethnicity may be a factor, activity levels which may also be related to cultural factors), physician factors (implant techniques) and lead factors (materials, construction). In addition to that, there is the potential bias of follow-up technique (remote vs in person and continuous vs intermittent). However, the difference between returned product analysis and a center analysis is significant and this points out the need for all manufactures to do a prospective analysis with follow-up.

Comparison with previous studies

Great controversy remains concerning the frequency of Linox lead dysfunction. A product performance report by Biotronik indicated a cumulative lead survival of 95.2%

229 at 7 years for the Linox S and 95.0% at 9 years for the Linox SD.[5] Good et al. recently
230 published large registries of Linox leads involving 2935 Linox leads and 998 Linox
231 smart leads. That study demonstrated a very low rate of mechanical lead failure
232 (survival rates: 96.3% at 5 years, 96.6% at 4 years, respectively), comprising 14
233 (0.36%) conductor failures, 10 (0.25%) insulation breaches and 8 (0.2%) cases of
234 abnormal pacing impedance.[8] However, among recently published data, almost all
235 studies reported from Europe and Western countries have suggested unacceptably high
236 rates of Linox lead failure. [6, 7, 9] A Canadian retrospective multicenter registry study
237 reported a 91.6% survival rate for the Linox lead at 5 years.[6] Moreover, a single-center
238 study of 93 patients reported a 5-year survival rate of 88% for the Linox lead.[7] Up until
239 now, however, no data have been available regarding the performance of Linox leads in
240 Asian populations. The survival probability of Linox leads in this study was also lower
241 than Biotronik reported from its own data (Table 4). Several factors may explain the
242 somewhat lower survival rate in our study. This prevalence of lead failure is probably
243 explained by a longer follow-up than the previous report and may be explained by
244 variable center failure rates and possible bias towards reporting of data from institutes
245 with higher failure rates. [8] Another explanation for the discrepancy between our results
246 and Biotronik data may be related to differences in the ethnicities of the different

cohorts. The present study was performed in Asia, whereas the largest Biotronik postmarket study is from the United States. The higher lead failure rate in this study also might be explained by differing population demographics, such as age, gender, and physical frame compared to the Biotronik study. Furthermore, it is notable that Biotronik and most companies have only failed analysis based on "returned product". Most leads never get returned, so unless the company has a chronic lead surveillance study, they are likely to significantly underestimate the true failure rates of their leads. Whatever the mechanism, more research is needed to understand why these differences exist among institutions.

Risk factors for lead failure

In our study, age at implantation was a predictor of Linox lead failure. Similarly, Noti et al. reported age at implantation as a predictor of lead failure.[7] Another study identified female gender as a predictor of lead failure.[6] Age at implantation was also likely to be a predictor in that study, but was not statistically significant.

Even though an examination showed no significant differences, passive lead was associated with a close to 4 fold increase in risk of Linox lead failure. This seems to suggest that passive lead fixation might modify the effect of ICD brands on failure

outcome. Then we performed additional analysis to predict ICD failure for all ICD brands, but passive lead fixation was not significantly associated with lead failure in this study. Either way, further study with larger sample size is needed to adjust for confounders and examine the effect modifiers.

Various predictors of lead failure were reported with the Fidelis lead, including younger age, female gender, center, noncephalic access, and history of previous lead failure.[10] The precise reasons underlying early lead failure among younger patients remain unclear. However, as speculated in regard to early Fidelis lead failure in younger recipients, one explanation may be that younger, more active adults with preserved left ventricular function, such as those with Brugada syndrome, hypertrophic cardiomyopathy, and congenitally corrected transposition of the great arteries with double switch operation, place greater stress on the Linox lead than older, more sedentary patients with reduced left ventricular function.

Mechanisms of early lead failure

For clinical reasons, lead extraction was attempted in only 2 patients in this study. The mechanisms underlying Linox lead failure thus remain unknown. In the two extracted leads, the cause of insulation defect seemed to be mechanical lead-to-can abrasion, not

283 “inside out” abrasion. Previous reports have described an association of conductor
284 externalization with electrical abnormality.[7,11,12] Noti et al. proposed performing
285 high-resolution fluoroscopic screening during generator replacement to check for the
286 presence of conductor externalization.[7,13] In our study, retrospective fluoroscopy did not
287 reveal any lead abnormalities, including conductor externalization. Without systematic
288 fluoroscopy screening, the rate of conductor externalization was obviously
289 underestimated. Causes of Linox lead failure were speculated to include insulation
290 injury and conductor fracture, because low and high lead impedance abnormalities and
291 non-physiological high rate sensing were recognized. The insulation and conductor in
292 the Linox lead may be more fragile than those in other ICD leads. Institutional or
293 operator-dependent factors can be excluded, because almost all lead implants in the 4
294 groups were performed by the same operators in a single institution, and during the
295 same era.
296
297 **Adverse events associated with lead failure**
298 Several large prospective randomized trials have demonstrated the safety, feasibility,
299 efficacy, and improved survival of RM. In addition, RM has allowed early detection of
300 adverse clinical events, such as arrhythmia, lead failure, and battery depletion.[14-15, 16] In

301 the present study, only one patient with Linox lead failure, who had been monitored by
302 wired RM, suffered from inappropriate ICD shock. Other lead failures were notified by
303 following wireless RM or in-office devices and were promptly managed, leading to a
304 lack of adverse clinical events. RM was thus very useful in preventing adverse events
305 such as inappropriate ICD shock in patients with lead failure. Our experience does not
306 support routine prophylactic replacement of normally functioning Linox leads.
307 Multicenter studies of a large number of patients should be conducted to clarify these
308 issues.
309
310 **Limitations**
311 Several limitations must be considered in relation to this study. First, the study was a
312 non-randomized retrospective analysis of a relatively small number of participants from
313 a single center. Especially, it is noteworthy that the Sprint Quattro leads cohort was too
314 small and the median follow-up period for the Sprint Quattro was shorter than that for
315 the other leads. In addition, the number for each lead models of Sprint Quattro and
316 Endotak Reliance would be low and may affect the statistics. Overall, only 19
317 defibrillation leads (9.3%) failed during the follow-up. Thus, we had insufficient
318 numbers of leads failure to conduct multivariate analysis. As noted above, a multicenter

study including a large number of patients should be conducted, and additional data are required before definitive guidelines can be adapted to the management of patients with Linox leads. Second, significant differences in baseline, procedural characteristics in our study population were seen among several types of ICD leads. In particular, mean duration of follow-up was shorter for the Sprint Quattro leads than for other leads. Third, for clinical reasons, lead extraction was only attempted in two patients in this study. As a result, the cause and type of lead failure were not able to be systemically verified.

CONCLUSIONS

In our single-center experience, the survival rate for the Linox lead was 81% at 7 years, representing a poor outcome comparable to that for the Sprint Fidelis lead (7-year survival, 77.2%). This is the first description of outcomes for Linox leads and the lead survival rate in an Asian population. The only predictor of Linox lead failure in our study was age at implantation, with age <58 years associated with increased risk of failure.

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REFERENCES

1. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The Task Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur heart J 2015;36:2793-2867.
2. Buxton AE, Ellison KE, Kirk MM, Frain B, Koo C, Gandhi G, Khouzam S. Primary Prevention of Sudden Cardiac Death: Trials in Patients with Coronary Artery Disease. Journal of Interventional Cardiac Electrophysiology 2003;9:203-206.
3. Urgent Medical Device information: Sprint Fidelis Lead Patient Management Recommendations. Minneapolis, MD:Medtronic Inc;October 14, 2007.
4. Medical SJ. Medical device advisory. Important product information up-date. http://www.sjmprofessional.com/Resources/product-notices-adviso-ries/riata-improtant-information-us.aspx 2011.
5. Biotronik. Product Performance Report July 2016. In;http//www. biotronik.com/files/A2ECD105C31DC0C5C1257F5000538E40/$FILE/Product%20Performance%20Report%202016-01.pdf.
6. Padfield GJ, Steinberg C, Karim SS, Tung S, Bennett MT, Le Maitre JP, Bashir J. Early failure of the Biotronik Linox implantable cardioverter defibrillator lead. J Cardiovasc Electrophysiol 2015;26:274-281.
7. Noti F, Lam A, Klossner N, Seiler J, Servatius H, Medeiros-Domingo A, Nam Tran V, Haeberlin A, Fuhrer J, Tanner H, Roten L. Failure rate and conductor externalization in the Biotronik Linox/Sorin Vigila implantable cardioverter-defibrillator lead. Heart Rhythm 2016;13:1075-1082.
8. Good ED, Cakulev I, Orlov MV, Hirsh D, Simeles J, Mohr K, Moll P, Bloom H. Long-Term Evaluation of Biotronik Linox and Linox(smart) Implantable Cardioverter Defibrillator Leads. J Cardiovasc Electrophysiol 2016;27:735-742.
9. van Malderen SC, Szili-Torok T, Yap SC, Hoeks SE, Zijlstra F, Theuns DA. Comparative study of the failure rates among 3 implantable defibrillator leads. Heart Rhythm 2016;13:2299-2305.
10. Hauser RG, Maisel WH, Friedman PA, Kallinen LM, Mugglin AS, Kumar K, Hodge DO, Morrison TB, Hayes DL. Longevity of Sprint Fidelis implantable cardioverter-defibrillator leads and risk factors for failure: implications for patient management. Circulation 2011;123:358-363.

11. Manfredi JA, Smithgall SM, Kircher CM, Lollis MA. Insulation failure with externalized conductor of a Linox SD lead: a case report. J Cardiovasc Electrophysiol 2014;25:440-441.
12. Howe AJ, McKeag NA, Wilson CM, Ashfield KP, Roberts MJ. Insulation Failure of the Linox Defibrillator Lead: A Case Report and Retrospective Review of a Single Center Experience. J Cardiovasc Electrophysiol 2015;26:686-689.
13. Erkapic D, Duray GZ, Bauernfeind T, De Rosa S, Hohnloser SH. Insulation defects of thin high-voltage ICD leads: an underestimated problem? J Cardiovasc Electrophysiol 2011;22:1018-1022.
14. Mabo P, Victor F, Bazin P, Ahres S, Babuty D, Da Costa A, Binet D, Daubert JC. A randomized trial of long-term remote monitoring of pacemaker recipients (the COMPAS trial). Eur heart J 2012;33:1105-1111.
15. Guedon-Moreau L, Lacroix D, Sadoul N, Clementy J, Kouakam C, Hermida JS, Aliot E, Boursier M, Bizeau O, Kacet S. A randomized study of remote follow-up of implantable cardioverter defibrillators: safety and efficacy report of the ECOST trial. Eur heart J 2013;34:605-614.
16. Slotwiner D, Varma N, Akar JG, et al. HRS Expert Consensus Statement on remote interrogation and monitoring for cardiovascular implantable electronic devices. Heart Rhythm 2015;12:e69-100.

Table 1. Baseline characteristics

	Linox (n=90)	Fidelis (n=37)	Quattro (n=27)	Endotak (n=50)	P
Follow-up (months) (median, 25th-75th percentile)	62.1 (31.9-77.7)	84.0 (58.9-109.3)	34.7 (26.3-56.6)	81.3 (32.9-126.3)	0.001
Age at implantation (years) (median, 25th-75th percentile)	58.0 (44.0-72.3)	56.0 (40.5-64.0)	60.0 (52.0-65.5)	55.5 (41.5-65.5)	0.215
Female gender	37.1% (n=34)	16.2% (n=6)	14.8% (n=4)	28.0% (n=14)	0.023
BMI (kg/m²)	23.1±3.85	22.6±4.49	22.3±3.14	22.2±4.30	0.77
Height (cm)	161.1±10.0	164.2±7.60	164.1±9.28	163.3±10.3	0.23
Body weight (kg)	60.3±13.3	61.0±12.3	60.5±11.2	60.5±14.2	0.995
Pathogenesis of cardiac	15.6%	18.9%	22.2%	12.0%	0.675

disease (coronary artery disease %)					
Primary prevention indication	48.9%	27.0%	44.4%	36.0%	0.11
Venous access (cephalic vein %)	52.2%	58.3%	57.7%	57.1%	0.67
Dual coil (%)	98.9%	97.3%	66.7%	89.8%	0.01
Passive lead fixation	47.8%	0.0%	25.9%	36.0%	0.001
Total no. of implanted leads (n)	2.33±0.76	2.03±0.72	2.40±0.93	1.98±0.59	0.012
Cardiac resynchronization therapy (%)	27.8%	21.0%	34.6%	8.0%	0.011
BNP (pg/ml)(median, 25th-75th percentile)	177.4 (87.8-461.5)	90.3 (14.8-328.7)	271 (64.1-654)	48.6 (13.6-153.4)	0.001
Cre (mg/dl)	0.95±045	1.36±1.44	1.28±1.22	1.05±1.30	0.17
LVEF (%)	46.5±19.6	51.4±20.3	35.4±17.6	57.5±17.1	0.01

Table 2. Details of Linox lead failure

Case	Age, sex	Pathogenesis of cardiac disease	ICD indication	Device	Lead model	Access	Lead age (months)	Type of failure	Electrical abnormalities	Presentation	Inappropriate shocks	Conductor externalization
1	55, F	HOCM	secondary	DDD	TD	Cephalic	63.4	Electrical abnormalities	Increased P/S impedance (Distal conductor 1743 Ω)	routine ICD control	no	no
2	73, F	HCM	primary	DDD	TD	Cephalic	35.7	Electrical abnormalities	Increased pacing threshold (3.0 V/0.4 ms)	routine ICD control	no	no
3	21, M	ccTGA	secondary	DDD	TD	Subclavian	26.4	Electrical abnormalities	Increased P/S impedance (>3000 Ω) Tip-ring 4000 Ω, tip coil 4000 Ω, ring coil 225 Ω	device alert	no	no
4	38, M	BrS	secondary	VVI	S	Cephalic	55.2	Non-physiological high rate sensing	Increased P/S impedance (1911 Ω)	device alert	no	no
5	25, M	BrS	primary	VVI	TD	Cephalic	30.3	Non-physiological high rate sensing	Increased P/S impedance (1713 Ω)	routine ICD control	no	no
6	45, M	DCM	primary	DDD	SD	Cephalic	59.5	Non-physiological high rate	Decreased P/S impedance (<200	device alert	no	no

								sensing	Ω) (Insulation abrasion S/O)			
7	49, F	DCM	primary	DDD	TD	Subclavian	56.4	Non-physiological high rate sensing	Increased P/S impedance(>3000 Ω)	device alert	yes	no
8	54, M	OMI	secondary	DDD	TD	Cephalic	22.6	Non-physiological high rate sensing	Increased P/S impedance (>2500 Ω), pacing threshold (3.0 V/0.4ms)	device alert	no	no
9	35, M	BrS	secondary	DDD	TD	Cephalic	79.7	Electrical abnormalities	High-voltage impedance <20 Ω	device alert	no	no
10	39, M	BrS	secondary	DDD	TD	Cephalic	59.6	Electrical abnormalities	Increased P/S impedance (1516 Ω)	device alert	no	no

402

403

404 Table 3. Predictors of lead failure in Linox leads

	Univariate	
Variable	HR (95%CI)	P
Age at implantation (≥58 years)	9.00 (1.13-71.3)	0.037
Female gender	0.74 (0.26-2.15)	0.58
BMI	1.02(0.97-1.10)	0.21
Cephalic access	0.38 (0.069-1.56)	0.161
Passive lead	3.91(0.85-18.7)	0.082
Total number of leads implanted	0.41 (0.16-1.08)	0.072
LVEF	1.02 (0.98-1.56)	0.305

405

406 Table 4. Summary of studies with estimated Linox lead survival data 5 years after

407 implantation

Study	**Number of leads in study (n)**	**Follow-up (median)**	**Survival rate (%)**			
			3 years	**4 years**	**5 years**	**7 years**
Product performance report (Biotronik)[5]	(15600†)	-	98.9	98.4	97.7	96.2
Good ED et al[8]	2935	3.6 years	98	96.9	96.3	-
Noti F et al[7]	93	3.4 years	-	-	88	-
Padfield GJ et al[6]	477	3.2 years	-	-	91.6	-
Van Malderen SC[9]	408	5.1 years	98.3		93.6	90.6
Present study	90	4.6 years	94.6	87.4	85.3	81

Figure legends

Figure 1. Kaplan-Meier curves of cumulative survival rates for Linox, Sprint Fidelis, Sprint Quattro, Endotak Reliance

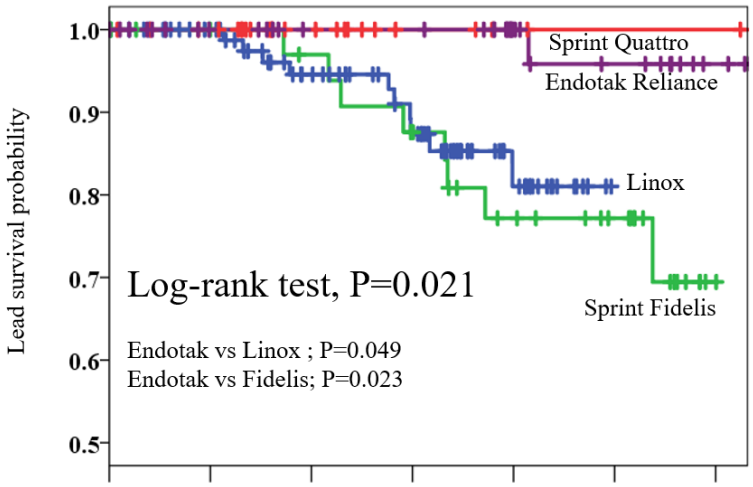
Figure 2. Temporary increased RV pacing impedance to out of range values in the setting of lead fracture.

Figure 3A. Exposed conductor with external abrasion

Figure 3B. Stored electrograms from patient No 4. Lead noise sensed inappropriately as ventricular fibrillation in the setting of lead fracture.

Figure 4. Survival of Linox ICD leads according to age

Figure 1.



Numbers at risk	.0	20.0	40.0	60.0	80.0	100.0	120.0	Follow-up (months)
Linox	90	79	61	47	18	—	—	
Sprint Fidelis	37	32	30	26	19	14	—	
Sprint Quattro	27	24	13	6	4	3	3	
Endotak Reliance	50	39	34	34	24	20	10	

Figure 2.

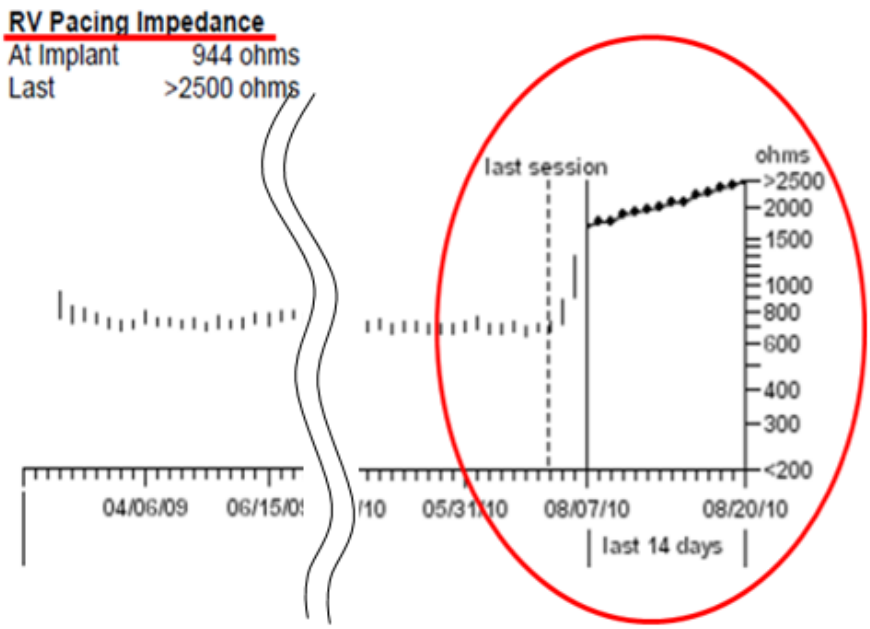
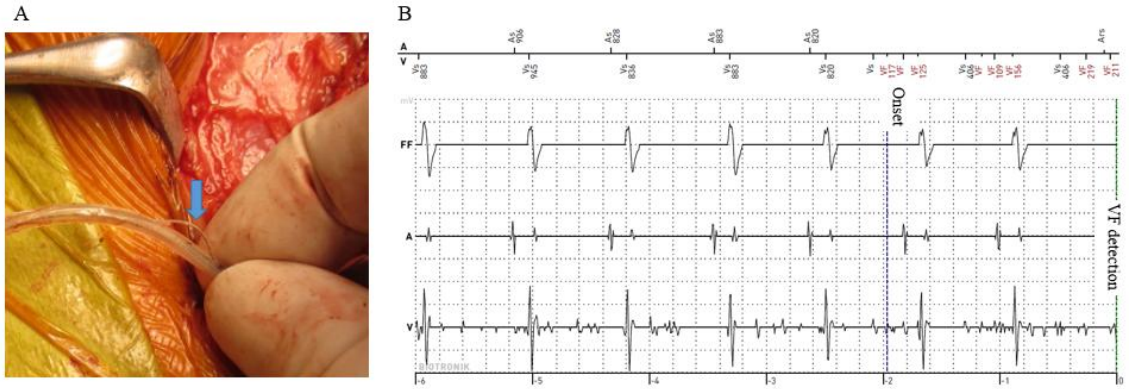
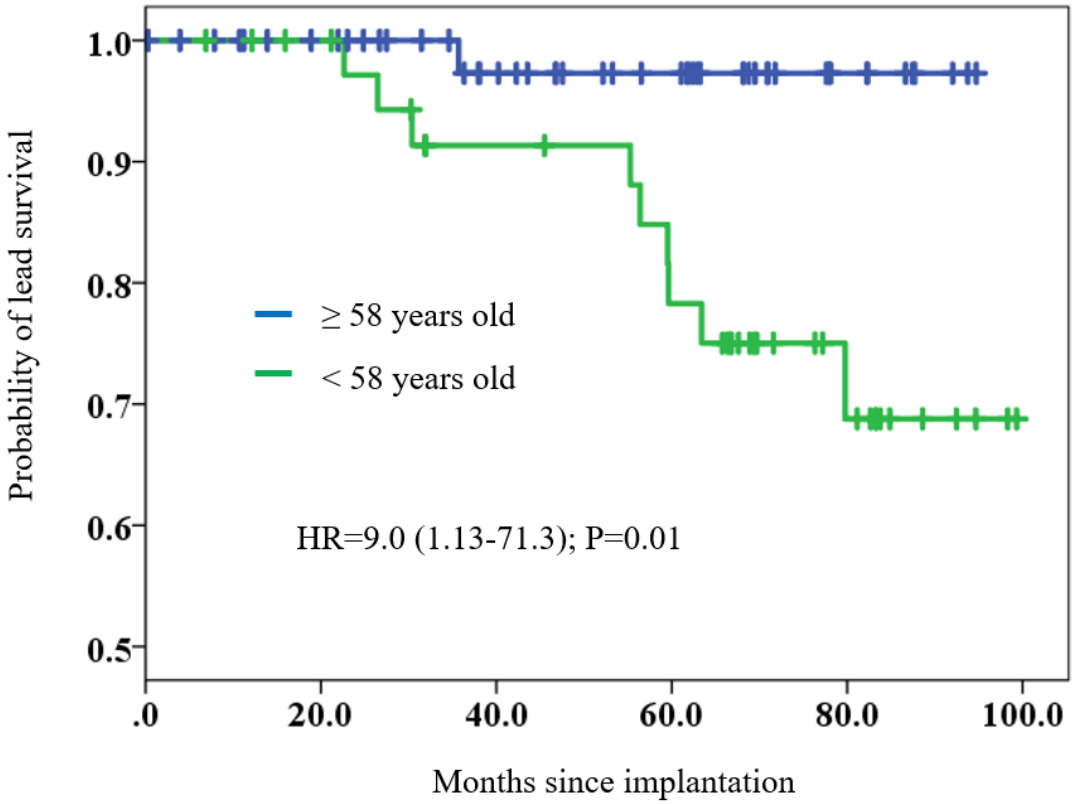


Figure 3A.

Figure 3B.



425 Figure 4.



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