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Safety, Handling and Electrical Performances of Bradycardia Leads in Acute Conditions: Results from the FINE Registry

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Abstract

Background: Beflex is an active fixation atrial and ventricular lead with a retractable screw; X-Fine is a passive fixation ventricular lead. These two bradycardia lead models were evaluated in the FINE study, an observational prospective trial conducted in France and Spain. Methods: Patients enlisted for pacemaker or defibrillator implants were enrolled. The primary objective was to assess acute dislodgement rates at the 3-month follow-up visit. Safety and electrical performances of the leads were assessed in acute conditions at implant and at the follow-up visit up to three months later. A handling questionnaire was submitted to implanting investigators immediately after implant. Results: A total of 2254 patients were enrolled in 95 centers; investigators implanted 1153 active atrial leads, mainly in the right atrium; 1021 active right ventricular leads, mainly in the septum and 712 passive right ventricular leads, mainly in the apex. After a mean follow-up of 54.9 ± 37.6 days, dislodgement rates were 1.0% and 1.6% for atrial and ventricular active, and 3.2% for ventricular passive leads. No unexpected adverse reactions were observed during the course of the study and the electrical performances at implant and follow-up visits remained within normal ranges. Overall, most investigators (84%) rated leads' handling as superior

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(better or best) to what observed with other bradycardia leads. Conclusion: Different bradycardia leads showed a dislodgement rate of 1.0% and 1.6% for atrial and ventricular active leads, and 3.2% for ventricular passive leads, at 3-month follow-up. Acute safety and electrical performances were within expected ranges and very good handling performances were observed.

Keywords

Bradycardia Lead, Acute Lead Performance, Lead Handling, Lead Safety, Active Fixation Lead, Passive Fixation Lead, X-Fine, Beflex

1. Introduction

With a broadening of the indications for bradycardia and tachycardia management and an aging population, the number of pacemakers and cardioverter defibrillators implants is increasing. There is also a shift toward the use of active-fixation leads, which offer the potential advantages of reduced lead dislodgment, rapid implantation and easier lead extraction compared to passive-fixation leads.

The FINE registry aimed to investigate short-term behavior of different bradycardia lead models: ventricular passive- and active-fixation and atrial active-fixation pacing leads.

2. Methods

2.1. Study Design

FINE (an observational study on XFine and Beflex bradycardia leads, ClinicalTrials.gov Identifier: NCT 01168518) was an observational prospective study conducted in 95 European centers (90% in France and 10% in Spain) evaluating XFine and Beflex bradycardia leads.

Included patients were those implanted with an endocavitary pacing lead (atrial and/or ventricular) connected to a single, double or triple chamber pacemaker or defibrillator. The implanted lead(s) had to allow the measurement of pacing capture threshold (PCT) at 0.5 ms, R-wave or P-wave amplitude and impedance of the lead(s). Patients were implanted with one or two of the leads under investigation. After enrolment, patients received their implant. Electrical lead performances were assessed at implant using a Program System Analyzer. A follow-up visit was scheduled one to three months after implant, to assess the device electrical performance, and report any lead dislodgment.

The study was declared to all competent authorities in France and Spain. Enrolled patients gave their informed consent and the study conduct complied with Good Clinical Practices and the Helsinki declaration.

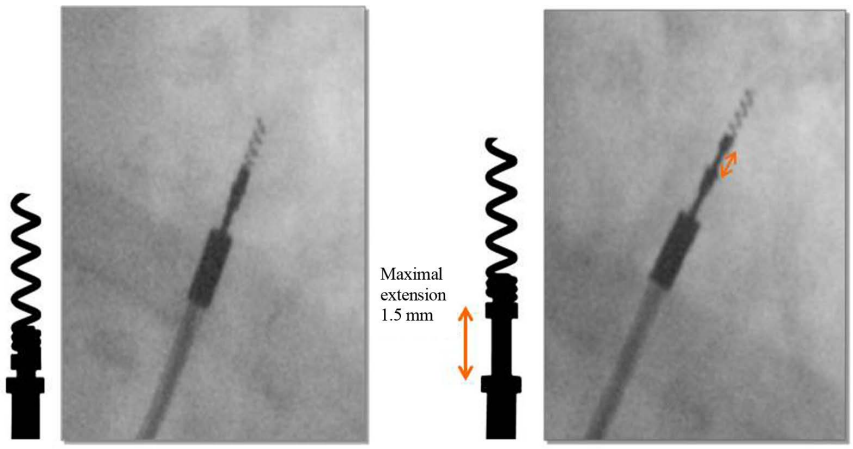
2.2. Study Objectives

The primary objective was the acute dislodgment rate of the leads during the study period (up to three months following implant).

Secondary objectives included a lead handling performance questionnaire filled-in by implanters and collected immediately after implant; the assessment of electrical performances (PCT, sensing amplitude and impedance) at implant (using a PSA) and at the follow-up visit (using the device). Adverse events were recorded throughout the study duration including extra or emergency visits.

2.3. Implanted Devices

The Beflex™ leads (Sorin CRM SAS, Clamart, France) is a bipolar, endocardial, 6-French lead body, steroid eluting, silicone insulated lead with an extendable (up to 1.5 mm)/retractable active-fixation helix for permanent pacing and sensing of either the atrium or ventricle (**Figure 1**). The lead is designed to be used with implantable cardiac pacemakers and defibrillators. In this steroid-eluting lead, a silicone elastomer collar containing 310 µg of dexamethasone sodium phosphate is located just behind the electrode tip. Upon exposure to body fluids, the steroid elutes progressively into the cardiac tissue around the electrode. These active straight leads can be used in the ventricle (RF46D model) or atrium (RF45D model).



Retracted screw (on the left) and extended screw (on the right)

Figure 1. X-ray visibility—Beflex™ leads.

The XFine™ passive straight ventricular leads (Sorin CRM SAS, Clamart, France) are endocardial leads with a 4.8 F lead body designed to be used with implantable cardiac pacemakers. They present a steroid-eluting lead, a silicone elastomer collar containing 1 mg of dexamethasone sodium phosphate located just behind the electrode tip. Two models were evaluated in the trial: 52 cm (TX 25D) and 58 cm (TX 26D).

The model of the pacemaker or defibrillator was left to investigators' discretion.

2.4. Statistical Analysis

For the primary objectives, the dislodgement rates were compared to pre-specified values, different for each type of lead, *i.e.*, 4% [1] for active atrial leads, 1.2% [2] for active ventricular leads and 0.7% [3] for passive ventricular leads. To reach a power of 95% for each test, and a type I error of 1.25%, adjusted with a potential rate of 10% lost to follow-up or missing data, estimated sample sizes were 750 atrial active leads, 806 ventricular active leads and 1070 ventricular passive leads.

Dislodgement was recorded when either reported as an adverse event or recorded in a specific field on the CRF. When dislodgement was reported without mentioning the type of lead (atrial or ventricular) on the adverse event or follow-up form, or reported as implanted in the ventricle, but without specifying if active or passive lead in the implant CRF, the following rules were applied:

- if the patient had one implant lead, the dislodgement was attributed to the implanted lead;
- if the patient had an unknown implanted ventricular lead, the dislodgement was attributed to both ventricular passive and active types;
- if the patient had more than one implanted lead (atrial or ventricular), the dislodgement was attributed to all the implanted leads.

The analysis was performed on the Intention-to-Treat (ITT) population including all patients with at least one successfully implanted lead. Descriptive statistics were used to present and summarize the data overall and by lead type (atrial active/ventricular active/ventricular passive). All tests for the primary endpoint were one-sided, and statistical significance was considered with a risk of 2.5%. No statistical test was performed when the mean value obtained exceeded the expected value.

3. Results

A total of 2886 leads were implanted in 2251 patients (**Table 1** presents the repartition by leads' model) between June 2008 and June 2010.

3.1. Lead Implantation

The lead access and positions are specified in **Table 1** and **Table 2**. Approximately 40% of the leads were implanted through the cephalic vein.

Table 1. Lead access at implantation.

	Atrial active (N = 1153)	Ventricular active (N = 1021)	Ventricular passive (N = 712)
Access vein			
Subclavian vein	690 (61.6%)	572 (57.5%)	422 (60.6%)
Cephalic vein	423 (37.8%)	423 (42.5%)	272 (39.0%)
Other	7 (0.6%)	-	3 (0.4%)
Missing data	33 (2.9%)	26 (2.5%)	15 (2.1%)
Access side			
Left	643 (65.8%)	526 (58.1%)	404 (64.9%)
Right	334 (34.2%)	379 (41.9%)	219 (35.1%)

Table 2. Lead position per model.

Position	Atrial active (N = 1153)	Ventricular active (N = 1021)	Ventricular passive (N = 712)
Atrial lateral wall	172 (15.7%)	/	/
Right auricle	872 (79.6%)	/	/
Ventricular apex	/	294 (29.9%)	677 (97.7%)
Ventricular septum	/	673 (68.5%)	5 (0.7%)
Other*	52 (4.7%)	16 (1.7%)	11 (1.6%)
Missing	57 (4.9%)	38 (3.7%)	19 (2.7%)

*Positioned in the wrong chamber.

General opinion on the lead handling was good. Overall most investigators rated the leads as "better" to implant compared to other models (general opinion on the lead implantation rated as "the best" or "better", according to the handling questionnaire results): 83.8% for the atrial active lead, 80.2% for the ventricular active and 90.0% for the ventricular passive leads. Detailed results on main items of the questionnaire are summarized in **Figure 2**.

3.2. Primary Objective

During a mean duration of 54.9 ± 37.6 days, 12 dislodgements (1.0%) were reported with the atrial active leads (95% confidence interval (CI): [0.5% - 1.6%], $p < 0.0001$, n = 1153); 16 dislodgements (1.6%) were reported with the right ventricular active leads (95% CI: [0.8% - 2.3%], n = 1021); 23 dislodgements (3.2%) were reported with the right ventricular passive leads (95% CI: [1.9% - 4.5%], n = 712). The required sample size of 1070 ventricular passive leads was not reached.

3.3. Secondary Objectives

Electrical performances of the leads are presented in **Table 3**. They remained within expected range up to the follow-up visit for the 3 models investigated.

While there was no device or procedure related death reported; six neither device-, nor procedure-related deaths (0.3%) occurred during the study (three cardiovascular deaths, one pulmonary death and one not specified). In addition to the dislodgements reported as SAEs and already analyzed in the primary endpoint, four procedure-related SAEs were reported (three pocket hematoma and one infection) and five SAEs neither device, nor procedure related occurred, including one cardiovascular in nature.

4. Discussion

The FINE registry is an observational, prospective, multicenter clinical investigation on bradycardia leads aiming

Table 3. Electrical performances of the leads at implant and at follow-up (between 1 and 3 months after implant).

	Pacing Thresholds	Impedance	Sensed Amplitude
	Atrial active lead, n = 1153		
At implant	0.92 ± 0.64 V	612.98 ± 169.52 Ω	3.12 ± 1.84 mV
Follow-up	0.69 ± 0.40 V	496.55 ± 123.29 Ω	3.18 ± 1.53 mV
	Ventricular active lead, n = 1021		
At implant	0.64 ± 0.34 V	794.16 ± 217.46 Ω	11.03 ± 5.53 mV
Follow-up	0.74 ± 0.50 V	602.53 ± 171.32 Ω	10.80 ± 3.69 mV
	Ventricular passive lead, n = 712		
At implant	0.43 ± 0.31 V	811.95 ± 256.28 Ω	12.24 ± 5.51 mV
Follow-up	0.66 ± 0.58 V	593.49 ± 137.16 Ω	11.21 ± 3.68 mV

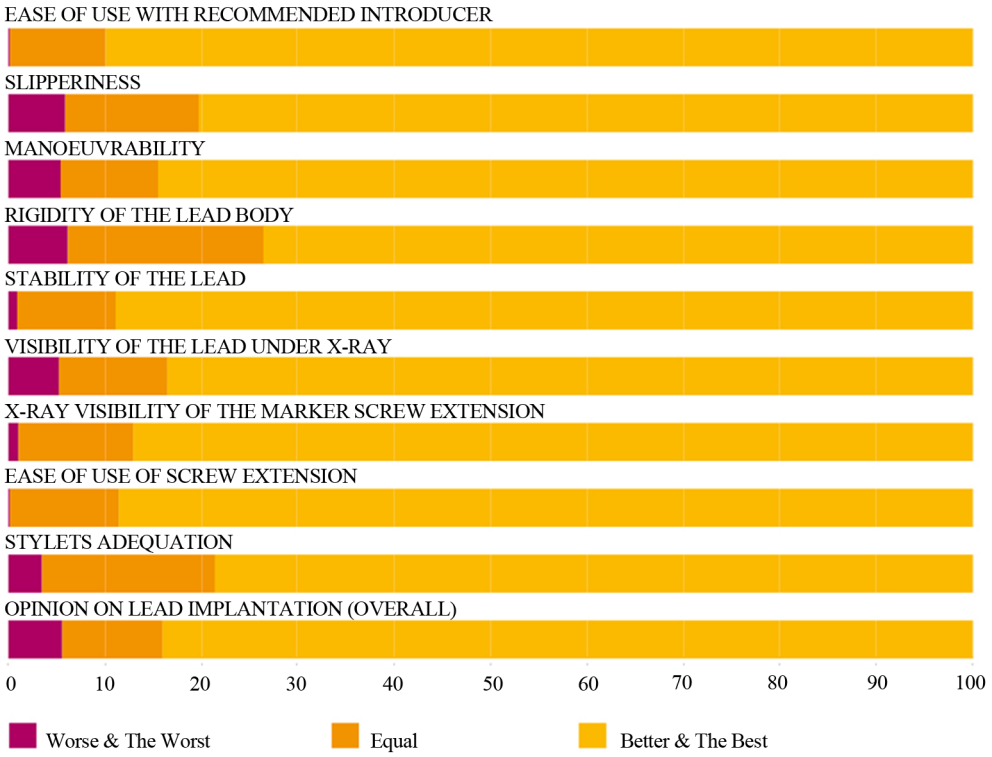


Figure 2. Results of the lead handling questionnaire collected at implantation.

to evaluate lead performances and safety in acute conditions. This post-market evaluation was conducted in 2254 patients implanted with 2886 leads in France and Spain from 2008 and 2010. Patients were followed-up for one to three months (one single follow-up visit). The dislodgement rates were respectively 1.0% for atrial, 1.6% for ventricular active and 3.2% for ventricular passive leads. No unexpected adverse reactions were observed during the course of the study and the electrical performances at implant and follow-up visits remained within expected ranges. The handling of the leads for highly rated by the implanters.

The dislodgment rates of the Beflex atrial and ventricular leads were as expected and within the range of the ones reported in the literature: within 30 days after implant, from 0.1% to 2.6% for the atrial lead [4]-[7] and from 0.3% to 1.7% [7] [8] for the ventricular lead. The XFine passive ventricular lead presented a higher dislodgment rate than expected (3.2%). However, it should be noted that, due to a lower inclusion rate as initially scheduled, the required sample size was not reached. Thus this section of the study did not attain a power of 95% to

support our results.

Electrical performances were within ranges retrieved in the literature for the atrium: PCT was comparable to values observed by Kistler *et al.* [9], P-wave amplitude were close to those reported by Rickard [6] and Cornacchia [10], and impedance values compared to those found by Kistler [9] and Lotze *et al.* [11]. In the ventricle, PCT values compared with those reported by Rickard [6] and Lotze *et al.* [11]; sensing amplitude were aligned with Nagatomo *et al.* [12] and Schuchert *et al.* [13]. Finally, impedances were close to those reported by Schuchert [13].

The ease with which a lead can be introduced into the cephalic vein depends on several factors including anatomical considerations, tortuosity; the vein's status; cardiologist's experience and lead trackability. In the FINE registry, approximately 40% of the leads were successfully implanted through the cephalic vein. Routing the leads by the cephalic vein can be an interesting option for cardiologists as it avoids subclavian ponction with all the possible complications, such as pneumothorax, hematoma, arterial injury and damage linked to costoclavicular crush. The success of using the cephalic vein should not be interpreted solely using percentage achievement rates in a quantitative way, but should also include the qualitative evidence that shows the incontestable facility of using this route.

5. Limitations of the Study

By design, the registry presents several limitations: e.g. no ongoing monitoring was performed, and it led to a large amount of missing data in the different parameters collected and important indication on the study population, such as demographics were not collected. Moreover, in the cases of missing/not comprehensible data, the most conservative approach was chosen and therefore, the incidence of lead dislodgment reported might be superior to the reality. Finally, the required sample size could not be reached for the XFine lead due to a low inclusion rate.

6. Conclusion

The three different bradycardia leads studied in the FINE registry showed a dislodgement rate of 1.0% and 1.6% for atrial and ventricular active leads, and 3.2% for ventricular passive leads, at 3-month follow-up. Very good handling performances were observed and acute safety and electrical parameters were within expected ranges.

Acknowledgements

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Conflict of Interest

The FINE registry wad sponsored by SORIN CRM SAS (Clamart, France).

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List of Abbreviations

AE	Adverse Event
CRF	Case Report Form
ECG	Electrocardiogram
PHD	Pre Hospital Discharge
PSA	Program System Analyzer
ITT	Intention-To-Treat
SAP	Statistical Analysis Plan
SD	Standard Deviation
M1	Month 1
M3	Month 3