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CLINICAL RESEARCH

Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time during cryoballoon ablation of atrial fibrillation: the SWEET-Cryo strategy

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Aims Cryoballoon pulmonary vein isolation (CB-PVI) offers similar efficacy to point-by-point radiofrequency PVI for patients with atrial fibrillation (AF), but generally with higher X-ray exposure. Strategies aimed at reducing fluoroscopy mostly rely on other costly imaging techniques, limiting their applicability. We designed a Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time during CB-PVI (SWEET-Cryo) strategy and analysed its impact on fluoroscopy use and acute procedural and clinical outcomes.

Methods and results We enrolled 100 patients with paroxysmal or persistent AF undergoing CB-PVI by two operators with different levels of expertise. Patients treated with the SWEET-Cryo strategy (prospective cohort; $n = 50$) or conventional fluoroscopy (retrospective control cohort; $n = 50$) were compared. When applied by the senior operator, the SWEET-Cryo strategy significantly reduced the mean fluoroscopy time (FT) (2.6 ± 1.25 vs. 20.3 ± 10.8 min) and mean dose area product (DAP) (5.1 ± 3.8 vs. 35.3 ± 22.3 Gy cm2) compared with those of the control group, respectively ($P < 0.001$). Significant reductions in FT (6.4 ± 2.5 min vs. 32.5 ± 10.05) and DAP (13.9 ± 7.7 vs. 92.3 ± 63.8) were also achieved by the less experienced operator ($P < 0.001$). No difference was observed in acute and long-term complications or freedom from AF between fluoroscopy strategies during a 33-month median follow-up. Mean FT was maintained below 3 min in randomly selected cases performed during the follow-up period.

Conclusion In contrast to conventional protocols and regardless of the operator's experience, the optimized SWEET-Cryo strategy dramatically reduced fluoroscopy exposure during CB-PVI. The efficacy, safety, or added costs of the ablation procedure were not compromised.

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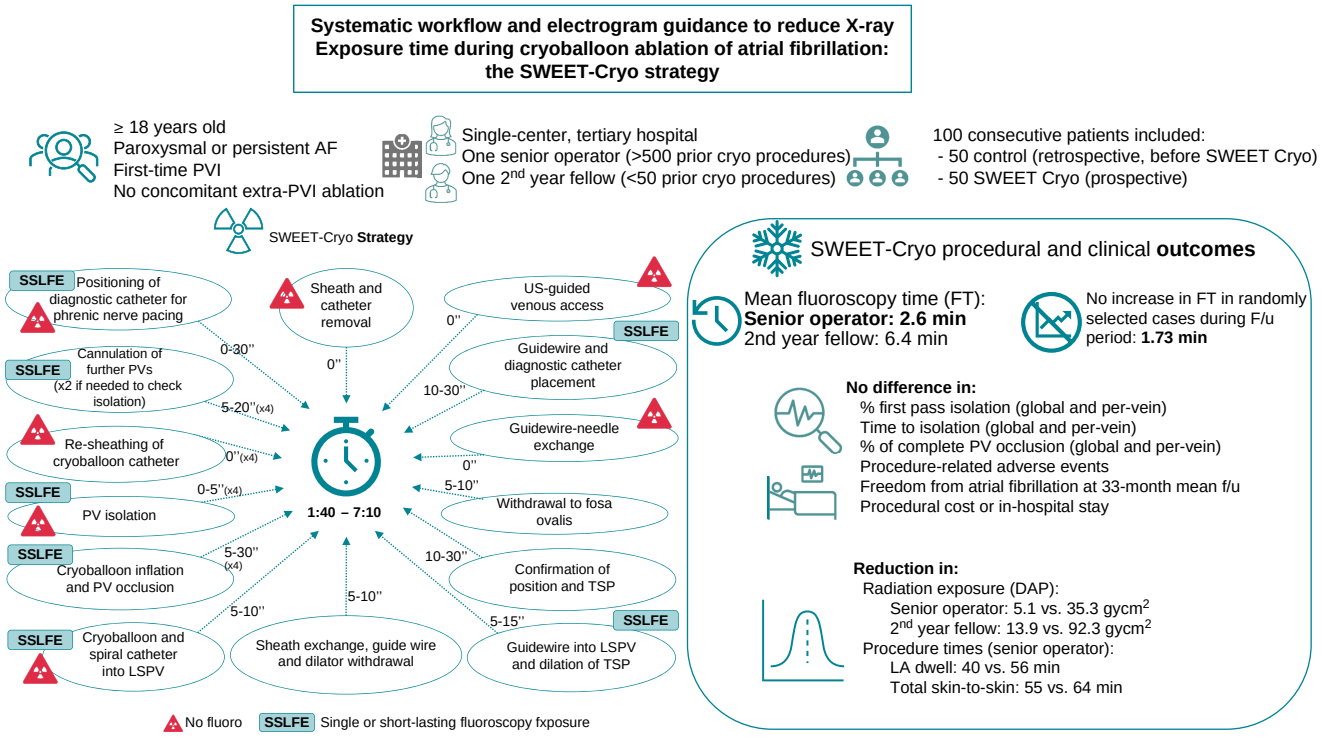
Graphical Abstract



Keywords Fluoroscopy • X-ray • Cryoablation • Atrial fibrillation • Pulmonary vein isolation

What's new?

- During cryoballoon atrial fibrillation ablation, the Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time during CB-PVI (SWEET-Cryo) strategy reduced X-ray exposure by more than 80% compared with the conventional use of fluoroscopy. This is the greatest reduction observed among optimized protocols that do not rely on non-fluoroscopic imaging modalities.
- The efficacy of the ablation procedure and rate of periprocedural complications with SWEET-Cryo were comparable with those reported in procedures with conventional X-ray imaging.
- The SWEET-Cryo strategy achieves important fluoroscopy reductions even among less experienced cryoballoon operators.
- SWEET-Cryo emerges as a new standard-of-care fluoroscopy usage protocol for cryoablation to systematically minimize radiation exposure to patients and operators with no associated costs.

Introduction

Atrial fibrillation (AF) is the most frequent cardiac arrhythmia encountered in clinical practice. Pulmonary vein isolation (PVI) is superior to antiarrhythmic drugs for rhythm control, arrhythmia-related symptoms, and delayed progression from paroxysmal to persistent AF.[1] Cryoballoon PVI (CB-PVI) is non-inferior to conventional point-by-point radiofrequency (RF) catheter ablation in terms of safety and freedom from AF, allowing single-shot applications, which shortens procedure times and operator's learning curves.[1,2]

The use of electro-anatomic mapping (EAM) is considered a standard in RF PVI, while CB-PVI relies mostly on fluoroscopy for catheter visualization, exposing the patient, the operator, and the rest of the staff to ionizing radiation.[3–7] Fluoroscopy reduction strategies in CB-PVI often require intracardiac echocardiography (ICE) or EAM navigation systems to replace X-ray in several phases of the ablation procedure. These significantly increase procedure costs and frequently prolong it, which limits their widespread use in electrophysiology laboratories.[8–11]

We developed a Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time during CB-PVI (SWEET-Cryo) without the use of any additional imaging methods. This study aimed to assess fluoroscopy exposure associated with the SWEET-Cryo strategy in contrast to conventional X-ray use during CB-PVI, and the comparative impact of both methodologies on other acute procedural parameters and long-term clinical outcomes.

Methods

Study design

The SWEET-Cryo study is a single-centre ambidirectional observational study with two cohorts (retrospective and prospective) of adult patients with AF subject to CB-PVI using two fluoroscopy imaging strategies.

Both the retrospective and prospective phases of the study were carried out in a tertiary University Hospital after receiving approval from the corresponding ethics committee. Patient data were handled according to the current General Data Protection Regulation 2016/679 of the European Parliament (EU-GDPR) and the Council of 27 April 2016 on Personal Data Protection as well as national and local regulations regarding patient autonomy, and rights and obligations in terms of information and clinical documentation.

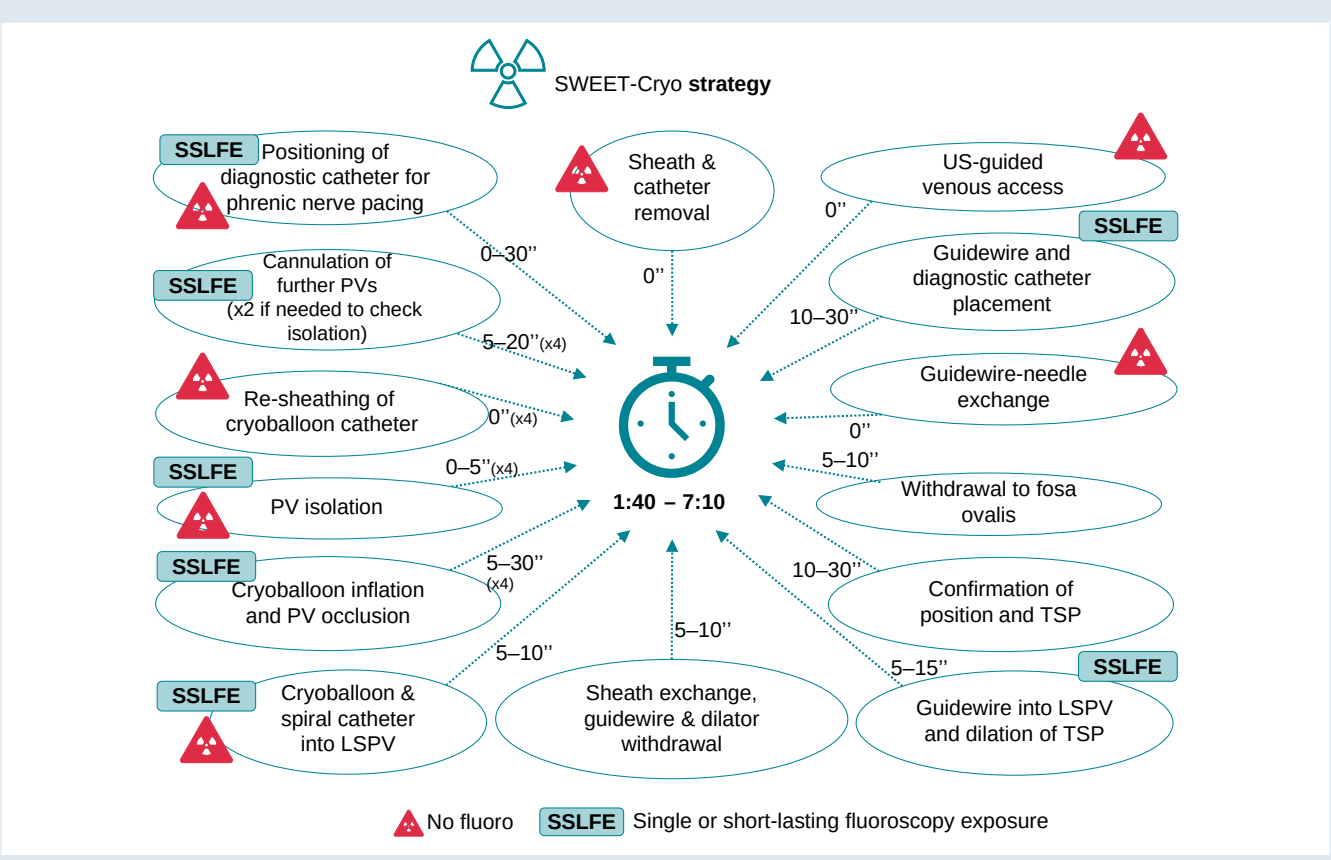


Figure 1 Steps in the cryoablation procedure where the SWEET-Cryo strategy for fluoroscopy reduction is applied. LSPV, left superior pulmonary vein; PV, pulmonary vein; RAO, right atrium occlusion; SVC, superior vena cava; TSP, transeptal puncture.

Ablation procedure

All patients underwent transoesophageal echocardiogram in the 48 h prior to the procedure to ensure freedom from left atrial (LA) thrombus, as per institution protocol. No other pre- or intra-procedural imaging techniques were performed. Oral anticoagulation was not interrupted, and a bolus of unfractionated heparin was administered immediately after transeptal (TS) puncture with an activated clotting time target ≥ 300 s. Femoral venous access was obtained under ultrasound (US) guidance, and a 4-pole deflectable Inquiry™ catheter and SL-0 sheath (both Abbott, Chicago, IL) were initially placed. Transeptal puncture was performed with a Brockenbrough BRK-1 needle (Abbott, Chicago, IL) under fluoroscopy, without any additional guidance techniques, and followed by placement of a J-tip guidewire in the left atrium to exchange the SL-0 sheath for the cryoablation kit (FlexCath sheath, ArcticFront Advance Pro cryoablation catheter, and Achieve 20 mm octapolar catheter, all Medtronic, Minneapolis, MN).

All procedures were performed with an Allura Xper (Philips N.V., Amsterdam, NL) system with fluoroscopy on electrophysiology mode and cinefluorographic acquisition (cine) at 7.5 ips in both cohorts. Cine runs were recorded in 30° left and right anterior oblique positions before TS puncture and to register contrast retention before cryoablation in each pulmonary vein (PV).

Setting

The prospective cohort was composed of patients who were treated following the SWEET-Cryo protocol during a 16-month period starting on 01 January 2020 (recruitment period). They were followed up for a minimum of 18 months until 30 November 2022 (end of the study). The strategy is based on three main pillars to reduce fluoroscopy: using electrograms (EGMs) and markers in the cryoablation materials as the main source of information to determine their position, systematic non-fluoroscopic handling of the catheters to cannulate PVs with use of fluoroscopy merely to confirm their position before proceeding to the next step, and replacing prolonged fluoroscopic exposures with short-lasting fluoroscopic exposures (SLFE) of <1 s. Regarding the latter, either single—to confirm catheter position—or multiple—to guide or confirm changes in handling—exposures were used as considered necessary by the operator.

Stepwise measures to reduce the use of fluoroscopy are depicted in *Figure 1*, and detailed information may be consulted in the Supplementary material online, *Figure S1*. Key aspects of this workflow are as follows: (i) US-guided femoral venous cannulation; (ii) attempting progression of a J-tip guidewire to the superior vena cava and a diagnostic catheter to the right atrium before first X-ray exposure; (iii) progression of a sheath for TS puncture over a guidewire replacing continuous fluoroscopy with single or short-lasting fluoroscopy exposures (SSLFE) until confirmation of sheath positioning in the superior vena cava; (iv) non-fluoroscopic progression of a TS needle inside the sheath; (v) after TS puncture, progression of a J-tip guidewire into the left atrium with SSLFE until confirmation of PV cannulation; (vi) dilation of the TS puncture orifice without fluoroscopic guidance; (vii) sheath exchange until the distal end of a steerable cryoablation sheath is at the PV ostium, guided by SSLFE instead of continuous fluoroscopy; (viii) progression of a cryoballoon catheter guided by markers on the catheter body without fluoroscopy; (ix) progression of a spiral diagnostic catheter inside the PV confirmed by decrease in EGM amplitude; (x) SSLFE to confirm the catheter position prior to cryoballoon inflation; (xi) cryoballoon inflation and sheath-balloon handling to occlude PV prior to fluoroscopy; (xii) SSLFE to confirm PV occlusion after inflation and contrast injection; (xiii) after each cryoenergy application, retrieval of the catheter inside the sheath guided by the marks on the catheter body and retrieval of the spiral catheter to the distal part of the sheath confirmed by the presence of noise on EGM of its proximal dipole; (xiv) SSLFE to confirm the degree of sheath deflection before transition to cannulate next PV; (xv) handling of the sheath for cannulation of the next PV and progression of the spiral catheter guided by EGMs and without the use of fluoroscopy; (xvi) repetition of steps (viii)–(xv) for each PV; and (xvii) placement of the diagnostic catheter for phrenic nerve pacing with minimal or no fluoroscopy using SSLFE.

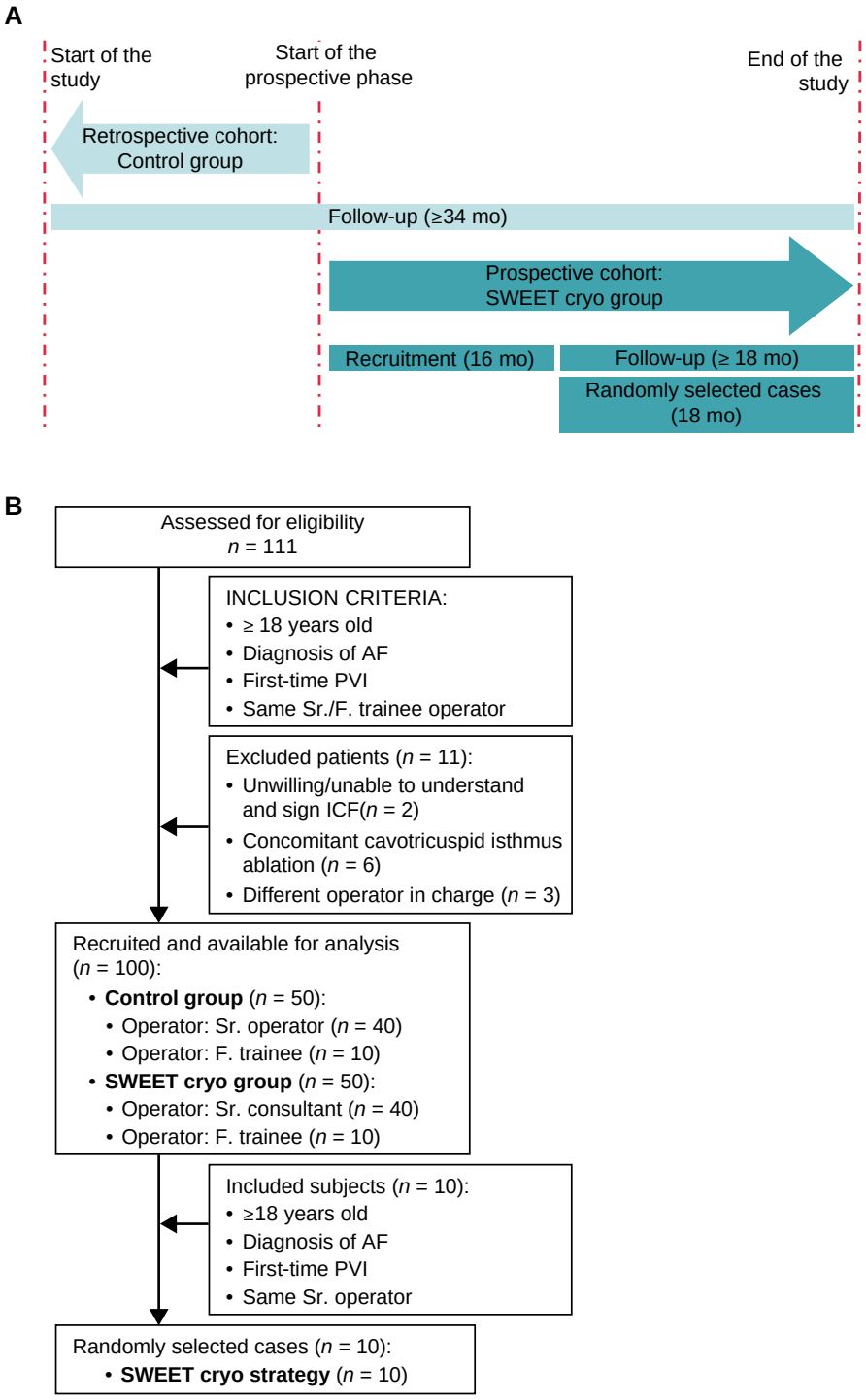


Figure 2 Study design (*A*) and flowchart (*B*). AF, atrial fibrillation; F., fellow; ICF, informed consent form; mo, months; Sr., senior; PVI, pulmonary vein isolation; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

The retrospective cohort included patients with AF who had undergone CB-PVI following the conventional operators' usual practice regarding X-ray guidance of the procedure (control group) before the start of the prospective phase. They were followed up for at least 34 months until the end of the study. AF ablation procedures in both cohorts were performed by the same two operators, who, at the time of study initiation, were a senior consultant with 6-year experience in electrophysiology and over 500 CB-PVI cases previously performed as the first operator and a second-year fellow trainee. A less senior operator was also included in the study design to evaluate the applicability of the protocol, and feasibility of reduction in radiation exposure, across all levels of expertise.

We anticipated a risk of better performance and, therefore, likely reduction of fluoroscopy time (FT) of both operators that could result from the awareness of being observed and participating in a study. To mitigate this

Table 1 Patient baseline characteristics

	All ($n = 100$)	Control group ($n = 50$)	SWEET-Cryo group ($n = 50$)	*P* value
Age, years	62.7 ± 11.3	60.6 ± 12.8	64.7 ± 8.8	0.07
Sex (male), %	69	72	66	0.52
BMI	27.7 ± 4.6	27.4 ± 4.6	27.4 ± 4.4	0.95
Hypertension, %	51	48	54	0.55
Diabetes mellitus, %	13	14	12	0.77
COPD, %	2	4	0	0.15
Stroke/TIA, %	3	4	2	0.56
Vascular disease, %	7	8	6	0.69
CHA2DS2-VASc score, %				
0	21	28	14	0.09
1	21	18	24	0.46
2	21	18	24	0.46
3	17	12	22	0.18
4	14	16	12	0.56
5	6	8	4	0.40
eGFR, mL/min/1.73 m^2	80 (64–90)	82 (64.7–90)	77.5 (59–90)	0.61
Cardiomyopathy, %				
None	57	60	54	0.55
Ischaemic	23	20	26	0.48
Tachycardiomyopathy	12	14	10	0.54
Non-ischaemic	4	3	5	0.61
Hypertensive	2	1	3	0.48
Other	2	2	2	1.00
Echocardiographic data				
LVEF, %	60 (46.5–63.2)	60 (42.5–62.5)	60 (49.2–66.2)	0.32
LA indexed volume, mL/m^2	41.5 ± 11.5	45 ± 10.6	38.5 ± 11.6	0.06
≥grade 2 mitral regurgitation, %	9	10	8	0.73
QRS width, %				
≤120 ms/>120 ms	95/5	96/4	94/6	0.65
AF, %				
Paroxysmal/persistent	53/47	60/40	46/54	0.16
Time from diagnosis of AF to ablation, %				
<1 year	40	30	43	0.18
1–5 years	38	38	38	1.00
>5 years	22	32	19	0.14
Anti-arrhythmic drugs, %				
Flecainide	24	30	28	0.83
Amiodarone	29	34	24	0.27
Dronedarone	8	12	8	0.51
None	39	24	40	0.09
Antithrombotic treatment, %				
DOACs	59	48	62	0.16
Warfarin/acenocumarol	28	34	22	0.18
None	13	18	16	0.79

For quantitative variables, values are expressed as mean ± SD or median [IQR] as appropriate. AF, atrial fibrillation; BMI, body mass index; CHA2DS2-VASc, congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female); COPD, chronic obstructive pulmonary disease; DOACs, direct oral anticoagulants; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LA, left atrial; LVEF, left ventricular ejection fraction; SD, standard deviation; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time; TIA, transient ischaemic attack.

Table 2 Intraprocedural parameters and AEs

	Control group ($n = 50$)	SWEET-Cryo group ($n = 50$)	*P* value
FT, min			
Operator: senior consultant	20.3 ± 10.8	2.6 ± 1.25	**<0.001**
Operator: fellow trainee	32.5 ± 10.1	6.4 ± 2.5	**<0.001**
DAP, Gy cm^2			
Operator: senior consultant	35.3 ± 22,3	5.1 ± 3.8	**<0.001**
Operator: fellow trainee	92.3 ± 63.8	13.9 ± 7.7	**<0.001**
CAK, mGy			
Operator: senior consultant	229.0 (118.0–314.0)	3.9 (0.3–34.4)	**<0.001**
Operator: fellow trainee	457.0 (67.8–792.0)	59.2 (0.7–109.1)	**0.02**
Skin-to-skin procedure time, min			
Operator: senior consultant	64 (60–80)	55 (45–60)	**<0.001**
Operator: fellow trainee	90 (76–107)	62 (60–71)	**0.02**
LA dwell time, min			
Operator: senior consultant	56 (50–70)	40 (31–49)	**<0.001**
Operator: fellow trainee	80 (65–97)	50 (45–52)	**0.003**
PV anatomy, %			
4 independent veins	90	88	0.75
Left common PV	6	8	0.70
Right intermediate PV	4	4	1.00
Complete PV occlusion before application, %			
Left superior PV	93.6	93.5	0.98
Left common PV	33.3	25.0	0.36
Left inferior PV	95.7	91.3	0.37
Right superior PV	96.0	92.0	0.70
Right intermediate PV	100.0	100.0	1.00
Right inferior PV	92.0	92.0	1.00
First-pass electrical isolation, %			
Left superior PV	95.7	95.6	0.98
Left common PV	33.3	25.0	0.36
Left inferior PV	91.5	95.6	0.41
Right superior PV	96.0	94.0	0.65
Right intermediate PV	100.0	100.0	1.00
Right inferior PV	96.0	88.4	0.16
Time to isolation, s			
Left superior PV[a]	46.8 ± 18.2	44,9 ± 20.8	0.79
Left inferior PV[a]	66.3 ± 54.5	62.0 ± 70.6	0.76
Right superior PV	44.8 ± 24.3	54.7 ± 33.3	0.14
Right intermediate PV	43.7 ± 33.5	44.4 ± 19.2	0.97
Right inferior PV	54.4 ± 62.0	45.7 ± 21.0	0.39
AEs, %			
Vascular complications	0	0	1.00
Minor bleeding at the puncture site	4	2	0.56
Transient phrenic nerve palsy	6	6	1.00
Cardiac tamponade	0	0	1.00
Stroke/TIA	2	0	0.32

Continued

Table 2 *Continued*

	Control group ($n = 50$)	SWEET-Cryo group ($n = 50$)	*P* value
Death	0	0	1.00
Total	12	8	0.51

For quantitative variables, values are expressed as mean ± SD or median (IQR) as appropriate. Statistically significant comparisons are indicated in bold. AEs, adverse events; CAK, cumulative air kerma; DAP, dose area product; FT, fluoroscopy time; IQR, interquartile range; LA, left atrial; SD, standard deviation; PV, pulmonary vein; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time; TIA, transient ischaemic attack.
[a]Including applications in the superior and inferior branches of left common pulmonary veins.

type of bias and assess the long-term applicability and results of this strategy, the same outcome measures were analysed in an extension study. This included 10 randomly selected cases performed during the 18-month follow-up period, which were retrospectively analysed.

Participants

The inclusion criteria were adult (≥18 years old) patients diagnosed with AF and subject to CB ablation for the first time by either the senior consultant or the fellow trainee operator under staff supervision. Patients of the prospective cohort were able to understand the nature of the study and provided their written consent to participate in it. The ethics committee waived the requirement for informed consent to obtain the procedural and follow-up information of the retrospective cohort. Exclusion criteria were any other concomitant procedures, such as cavo-tricuspid isthmus ablation or electrophysiological study.

Patients of both cohorts were recruited consecutively from the start date of the prospective phase onwards (prospective cohort) or backwards (retrospective cohort). The cohort for the extension study was comprised of subjects who fulfilled the same eligibility criteria except that they were only managed by the senior operator. These patients were managed with the SWEET-Cryo strategy, which continued to be routinely applied by the senior operator (*Figure 2*). Patients eligible for inclusion in the extension study who underwent cryoballoon ablation in the 18-month follow-up period were assigned consecutive numbers. Among those patients, 10 were randomly selected using a computer-based random number generator. This system is based on a complex computer's clock-based algorithm through the 'Math.random' method within JavaScript programming language. All 10 patients were contacted and gave informed consent to participate in the extension study.

Variables and data sources

Demographic parameters and medical history

The following baseline parameters were analysed in both cohorts of patients: age, sex, body mass index, history of hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), stroke or transient ischaemic attack (TIA), cardiomyopathy (ischaemic, non-ischaemic, hypertensive, tachycardiomyopathy, or others), and AF (paroxysmal or persistent), previous AF ablation, time from diagnosis of AF to ablation, estimated glomerular filtration rate, and echocardiographic (left ventricular ejection fraction, LA indexed volume, and mitral regurgitation) and electrocardiographic data (QRS width). Congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled), vascular disease, age 65 to 74 and sex category (female) (CHA2DS2-VASc) score was also collected.

Demographic and baseline medical parameters and all other retrospective data were obtained from patients' medical records, which had been anonymized before the analysis. For the prospective cohort, participants' data collected during the study were added to an electronic case report form with a unique identification code and limited access for authorized personnel.

Intraprocedural parameters

Total FT, radiation dose monitoring by dose area product (DAP) and cumulative air kerma (CAK) methods, skin-to-skin procedure time, and LA dwell time per type of operator (senior consultant and fellow trainee) were assessed. Other intraprocedural ablation parameters included PV anatomy (four independent veins, left common PV, and right intermediate PV), complete PV occlusion before application, and electrical isolation achieved during the first cryoablation and in every PV.

Periprocedural clinical parameters

Acute adverse events (AEs) during and after the procedure were analysed, including vascular complications, minor bleeding at the puncture site, transient phrenic nerve palsy, cardiac tamponade, stroke or TIA, and death.

The postprocedural parameters that were monitored during the follow-up period in both cohorts were the occurrence of AF, a second ablation procedure, the number of reconnected PVs observed at a redo procedure, and the use of antiarrhythmic medication. Follow-up visits were scheduled at 3, 6, 12, and 18 months after the index procedure, and every 6 months after that. Antiarrhythmic drugs were used at the discretion of the treating physician.

Outcome measures

The primary endpoint was the exposure to X-ray during AF ablation according to the fluoroscopy strategy followed (SWEET-Cryo vs. control) and the two operators with distinct seniority levels, as expressed by the total FT, DAP, and CAK. The secondary endpoints were the efficacy of the SWEET-Cryo strategy applied to CB-PVI according to intraprocedural parameters and its safety (acute AEs and postprocedural clinical outcomes) in contrast to CB-PVI with the conventional fluoroscopy approach. In the extension study cohort to assess the long-term application of the SWEET-Cryo strategy, the impact on fluoroscopy use (FT and DAP), procedure time and LA dwell time were evaluated.

Study size

Based on previous studies, the average FT achieved with optimized fluoroscopy protocols is 10 ± 6 min for AF ablation procedures with CB and no additional imaging techniques.[12] Here, we calculated a sample size of 100 patients based on a mean estimated FT of 6 min for those treated with the SWEET-Cryo strategy, with a 5% significance level ($P < 0.05$) and a power of 80% to detect differences between the two cohorts. No drop-out events affecting the primary endpoint were expected.

Statistical methods

Continuous variables were expressed by the mean and standard deviation or the median and interquartile range, depending on whether they followed a normal distribution (Kolmogorov–Smirnov test). Univariate comparative analyses were performed using Student's *t*-test or, for variables with non-normal distribution, the Mann–Whitney *U* test. Categorical variables are presented as percentages. The chi-squared or Fisher's exact tests were applied to compare their means, as appropriate. A pre-specified subgroup analysis was done according to both types of operators (senior consultant and fellow trainee). Multivariate regression analysis was performed to identify predictive factors for FT and DAP. The incidence of AF after ablation was estimated by the Kaplan–Meier method, and differences between study groups were analysed by the log-rank test after a 5-week blanking period during which recurrence of atrial tachyarrhythmias was not considered as treatment failure. For all tests, statistical significance was defined by $P < 0.05$. All analyses were performed using IBM's Statistical Package for the Social Sciences (SPSS®) for Windows version 22.

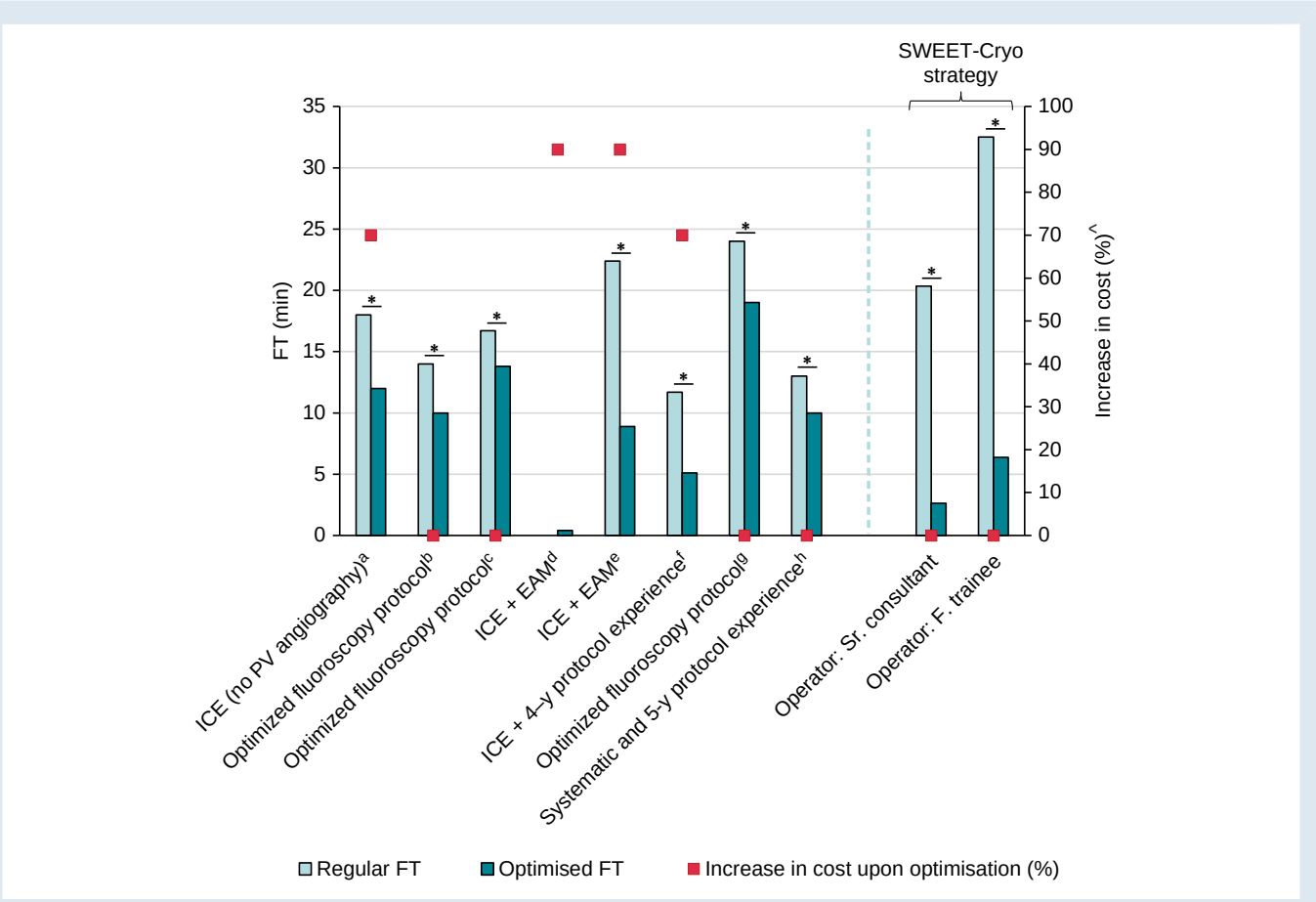


Figure 3 Impact of optimized protocols on FT reduction and associated cost increase for CB-PVI. On the right-hand side, mean FT with the SWEET-Cryo strategy applied by a senior operator ($n = 40$) or a fellow trainee ($n = 10$) in contrast to the conventional fluoroscopy protocol [senior operator ($n = 40$) vs. fellow trainee ($n = 10$)]. On the left-hand side, achieved FT reduction in previous reports based on fluoroscopy protocol optimization with or without concomitant use of non-fluoroscopic imaging techniques. Mean or median FT values are shown according to the source publication: [a]Rubesch-Kütemeyer *et al.*, 2016 (mean; retrospective observational study)[8]; [b]Reissmann *et al.*, 2018 (median; prospective controlled study)[13]; [c]Wieczorek *et al.*, 2020 (mean; prospective controlled study)[2]; [d]Reiss *et al.*, 2020 (median; retrospective observational study)[9]; [e]Maalouf *et al.*, 2020 (mean; retrospective observational study)[10]; [f]Rubesch-Kütemeyer *et al.*, 2020 (mean; retrospective observational study)[11]; [g]Holl *et al.*, 2021 (median; prospective controlled study)[14]; [h]Bordignon *et al.*, 2021 (mean; retrospective observational study).[12] *Statistically significant; ^based on the use of additional EAM or ICE and their associated costs (EUR 690 and EUR 2160, respectively), and considering one cryoablation kit per patient as baseline costs (EUR 3000 as per 2022 analytical accounts in the study centre); AF, atrial fibrillation; EAM, electroanatomic mapping; F., fellow; FT, fluoroscopy time; ICE, intracardiac echocardiography; Opt., optimized; PV, pulmonary veins; CB-PVI, cryoballoon pulmonary vein isolation; Sr., senior; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

Results

Baseline patient characteristics

A total of 111 patients were assessed for eligibility. After excluding 11 of them, 100 participants were recruited for the study. Of them, 50 participants in the control group underwent CB-PVI with the conventional fluoroscopy strategy. The remaining 50 participants belonged to the SWEET-Cryo group. In each study group, a fifth of the patients was treated by the fellow trainee operator. None of the participants was lost to follow-up (*Figure 2*).

Patient baseline characteristics are shown in *Table 1*. The majority presented with paroxysmal AF (53%), whereas no cases of permanent AF were enrolled. No significant differences in demographic or clinical history variables between cohorts were found.

Fluoroscopy exposure and efficacy of pulmonary vein isolation

During the CB-PVI procedures coupled to the SWEET-Cryo strategy and performed by the senior operator, the mean FT (2.6 ± 1.25 vs. 20.3 ± 10.8 min), mean DAP (5.1 ± 3.8 vs. 35.3 ± 22.3 Gy cm^2), and median CAK [3.9 (0.3–34.4) vs. 229.0 (118.0–314.0) mGy] were significantly reduced compared with those using the conventional fluoroscopy protocol, respectively ($P < 0.001$). Reductions observed in the fellow trainee subgroup analysis were consistent (*Table 2* and *Figure 3*). Moreover, the multivariate analysis revealed that, among several clinical and demographic covariates, the application of the SWEET-Cryo protocol for cryoablation was the only significant predictor for FT [odds ratio (OR): 0.01; 95% confidence interval (CI) < 0.01–0.02, $P < 0.001$] and DAP (OR: 0.01; 95% CI < 0.01–0.06), $P < 0.001$) in this study (*Table 3*).

Table 3 Multiple linear regression analysis of radiation exposure predictors

	FT			DAP		
Covariate	OR	95% CI	*P* value	OR	95% CI	*P* value
Age	0.31	0.1–3.4	0.07	1.17	0.6–2.1	0.62
BMI	1.91	0.5–7.3	0.34	2.99	1.1–8.3	**0.04**
Persistent AF	1.47	0.1–15.8	0.75	1.07	0.2–5.4	0.93
LA volume	1.62	0.6–4.4	0.34	1.23	0.6–2.5	0.57
LVEF	0.64	0.1–10.9	0.76	1.14	0.1–9.8	0.9
Mitral valve disease	0.56	0.2–16.4	0.74	1.16	0.1–12.4	0.93
SWEET-Cryo strategy	0.01	<0.01–0.02	**<0.001**	0.01	<0.01–0.06	**<0.001**

Statistically significant variables are indicated in bold. AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; DAP, dose-area product; LA, left atrial; LVEF, left ventricular ejection fraction, OR, odds ratio; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

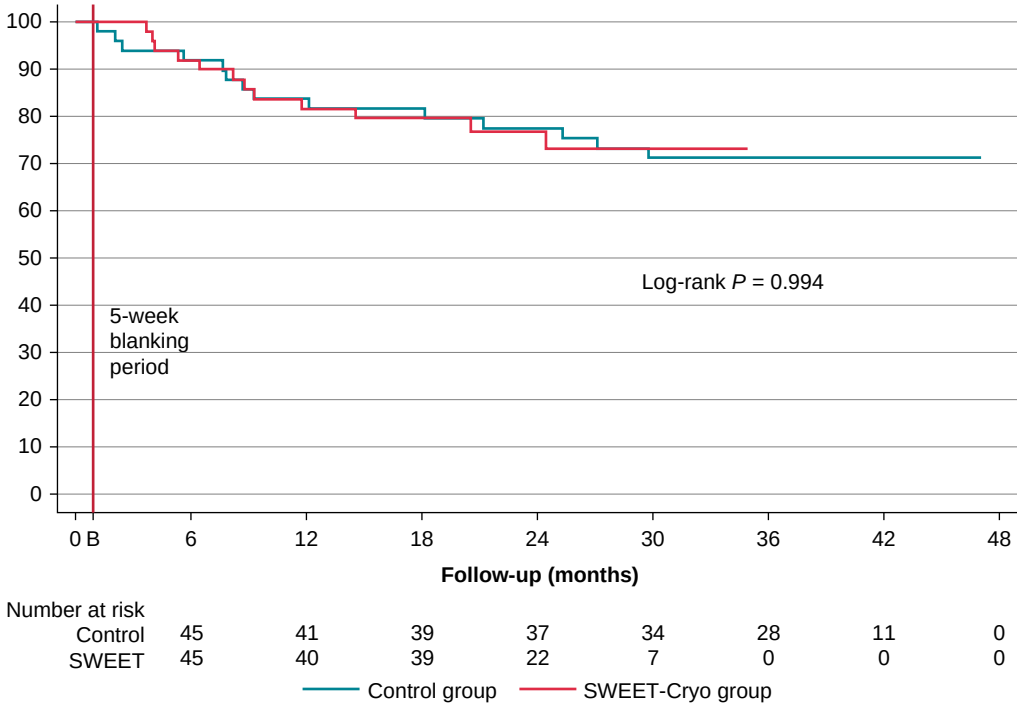


Figure 4 Kaplan–Meier estimates of AF recurrence-free survival after CBI-PVI. AF, atrial fibrillation; CB-PVI, cryoballoon pulmonary vein isolation; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

Other intraprocedural times were significantly reduced with the SWEET-Cryo strategy applied by the senior consultant, namely, the skin-to-skin [55 (45–60) vs. 64 (60–80) min] and the LA dwell [40 (31–49) vs. 56 (50–70) min] times, respectively ($P < 0.001$). We did not obtain further differences in intraprocedural efficacy parameters between fluoroscopy strategies or operators (*Table 2*).

Clinical outcomes

The most common acute AE in the whole study population was transient phrenic nerve palsy during the procedure. No deaths occurred in any of the procedures. We did not detect any significant differences between cohorts for these or any other AE (*Table 2*).

During a median follow-up period of 33 (24–39) months for all study patients, there were no significant differences regarding the freedom from AF recurrence in both study groups ($P = 0.994$ by log-rank test) (*Figure 4*). Approximately half (49%) of them required antiarrhythmic treatment after the first ablation, with a higher proportion in the control group (60% vs. 38%, $P = 0.03$), and 12% underwent a second procedure. Freedom from AF was not inferior among patients treated following the SWEET-Cryo strategy (*Table 5*).

Extension study

Ten patients (80% male, 65.3 ± 7.5 years old) were included in the extension study (*Table 4*). FT [1.73 (0.97–3.43)] and DAP [5.2

(2.7–9.3)] were similar to those reported in the main study cohort. Interestingly, FT was consistently short across procedures, with 60% and 80% of cases below 2 and 3.5 min, respectively (*Figure 5*).

Table 4 Fluoroscopy use and procedural duration in an extension analysis

	SWEET-Cryo strategy $n = 10$
Age, years	65.3 ± 7.5
Sex (male), %	80
BMI	27.3 ± 3.5
Cardiomyopathy, %	
Persistent AF	50
Tachycardiomyopathy (suspected)	30
Moderate mitral regurgitation	20
Echocardiographic data	
LVEF, %	52.3 ± 17.1
LA indexed volume, mL/m^2	35 ± 10.3
FT, min	
Operator: senior consultant	1.73 (0.97–3.43)
DAP, Gy cm^2	
Operator: senior consultant	5.2 (2.7–9.3)
Skin-to-skin procedure time, min	
Operator: senior consultant	59 ± 14
LA dwell time, min	
Operator: senior consultant	49 ± 13

Randomly selected procedures using the SWEET-Cryo strategy were analysed during an 18-month period following the prospective phase of the main study. For quantitative variables, values are expressed as mean ± SD or median (IQR) as appropriate. AF, atrial fibrillation; BMI, body mass index; DAP, dose-area product; FT, fluoroscopy time; IQR, interquartile range; LA, left atrial; LVEF, left ventricular ejection fraction; SD, standard deviation; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

Discussion

This study presents a simple strategy for catheter guidance during CB-PVI that reduces occupational and patient exposure to X-rays without affecting the efficacy and safety of the procedure.

The cumulative harmful effects of X-rays as class I carcinogens are well known, and effective zero or minimal X-ray procedures are pursued to protect interventional cardiologists and patients.[15] Here, we show that by using a simple fluoroscopy reduction strategy, we could reduce FT by more than 80% in comparison with the conventional approach, which translated into an over 80% decrease in radiation exposure parameters. Two main features characterize this strategy: using EGMs and catheter landmarks as main sources of information during catheter positioning and eliminating X-ray guidance during standard manoeuvres that do not require continuous visualization of catheter motion. Importantly, it does not prolong the procedure nor increase its complexity or cost, aspects which may have limited the adoption of other fluoroscopy reduction strategies proposed in the past. Both acute effectiveness, assessed by first-pass isolation rates, and long-term clinical efficacy were comparable in both groups. Both total procedure and LA dwell times were slightly decreased in the SWEET-Cryo group. We interpret this as most likely due to the effect of direct observation on operators' performance, but it may be argued that a clearly defined systematic approach and focusing on a single source of information at a time increase efficiency.

Following the results of several randomized trials showing similar efficacy between RF and CB ablation of AF, higher FT have repeatedly been pointed out as a drawback of CB.[4–6] Strategies to reduce radiation exposure in RF ablation continue to achieve a progressive decline in FT with advances in EAM systems.[16–18] However, the parallel decrease initially observed in CB ablation seems to have found a plateau of ∼15–18 min FT, as reported in randomized clinical trials and observational studies reporting standard practice in high-volume centres (*Figure 6*).[4–7,19–23]

Often, strategies to minimize fluoroscopy utilization during CB-PVI have relied on non-fluoroscopic imaging methods. Of note, Reiss *et al.* and Rubesch *et al.* obtained mean FT of 0.61 and 6.7 min in their 2020 reports, respectively,[9,11] the downside of which being the high costs associated with the use of ICE and 3D navigation to confirm balloon location (*Figure 3*). Reissmann *et al.* and Wieczorek *et al.* presented modified protocols that achieved reduced radiation exposure down to a median FT of 10 and a mean FT of 13.8 min with no additional imaging techniques, respectively.[2,13] More recently, the Frankfurt institutional approach for second-generation CB and

Table 5 Postprocedural clinical outcomes

	All ($n = 100$)	Control group ($n = 50$)	SWEET-Cryo group ($n = 50$)	*P* value
Follow-up duration, months	33 [24–39]	39 [37–43]	24 [20–29]	**<0.001**
Freedom from AF at the end of the follow-up period, %	70	68	72	0.66
Second ablation procedure during follow-up, %	12	14	10	0.54
No. of reconnected PVs observed at redo procedure, *n*	10	5	5	1.00
Antiarrhythmic drug treatment during follow-up, %	49	60	38	0.03
Flecainide	27	34	20	0.12
Amiodarone	19	22	16	0.45
Dronedarone	3	4	2	0.56

For quantitative variables, values are expressed as median (IQR). Statistically significant comparisons are indicated in bold. AF, atrial fibrillation; IQR, interquartile range; PV, pulmonary vein; SWEET, Systematic Workflow and Electrogram guidance to reduce X-ray Exposure Time.

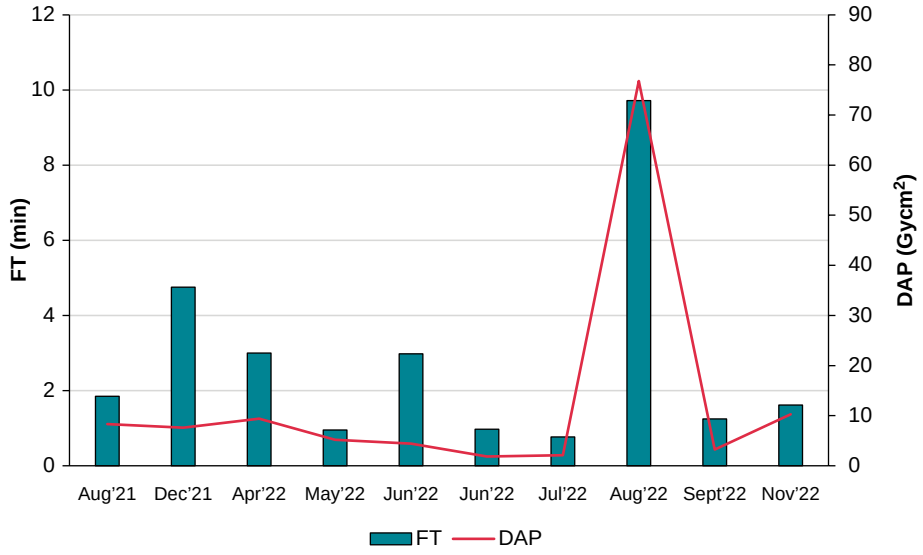


Figure 5 FT and radiation dose of randomly selected procedures during the 18-month follow-up period. DAP, dose-area product; FT, fluoroscopy time.

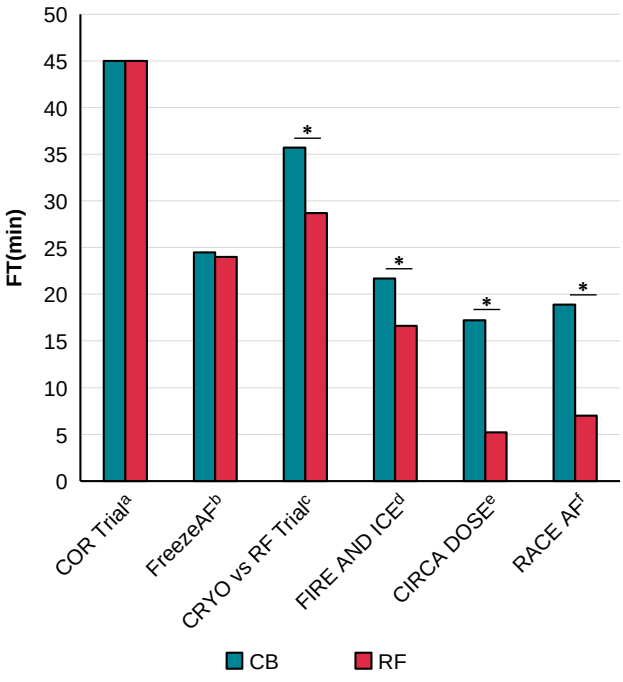


Figure 6 FT across previous randomized clinical trials comparing RF vs. CB ablation of AF. [a]Pérez-Castellano *et al.*, 2014[19]; [b]Luik *et al.*, 2015[20]; [c]Hunter *et al.*, 2015[4]; [d]Kuck *et al.*, 2016[5]; [e]Andrade *et al.*, 2019[6]; [f]Sorensen *et al.*, 2021.[7] *$P < 0.001$. AF, atrial fibrillation; CB, cryoballoon; FT, fluoroscopy time; RF, radiofrequency.

fluoroscopy use by Bordignon *et al.* yielded a mean FT of 11.0 min.[12] However, to the best of our knowledge, SWEET-Cryo is the protocol that implies the least fluoroscopy usage among all published optimizations that exclusively rely on X-ray imaging (*Figure 3*). Importantly, we also observed that FT and DAP can be reduced when less experienced operators apply the SWEET-Cryo protocol, which most likely indicates that it does not necessarily require a long learning curve or expertise.

The advent of pulsed-field ablation (PFA) systems brings about new challenges in fluoroscopy reduction. Recent trials have reported FT ranging from 13.7 ± 7.8 to 28 ± 9 min depending on the system used.[24–26] Despite the differences in catheter design and workflow, several

concepts introduced in the SWEET-Cryo strategy may help reduce X-ray exposure in PFA procedures.

To rule out the possible effect of several confounders in our results, the multivariate analysis confirmed that only the SWEET-Cryo strategy had a positive impact on fluoroscopy exposure. Finally, the sustained minimal FT and DAP values collected in the extension study cases provide evidence of the judicious use of the protocol outside a clinical study. Altogether, our positive findings strongly support the systematic implementation of the SWEET-Cryo protocol in routine ablation procedures to significantly contribute to the ongoing quest for minimal X-ray exposure in electrophysiology.

Limitations

One major limitation is the retrospective nature of the control group. However, it did not seem ethical to prospectively expose patients to more radiation than possibly necessary. On the other hand, the single-centre study design and relatively low number of participants were strengthened by a long follow-up period for both cohorts and the reports of 10 additional cases. Another limitation is that the cost increases associated with the different imaging techniques represented in *Figure 3* are approximate and based on our centre's 2022 analytical accounting. National health systems are very varied on a global scale, and it is beyond the scope of this study to perform any precise economic simulations. Finally, the reduction in DAP and CAK was limited due to the use of cine for the storage of selected images.

Conclusions

The SWEET-Cryo strategy achieves the lowest fluoroscopy use reported to date during cryoballoon ablation of AF with no additional imaging techniques. It does not increase cost nor impact safety and efficacy. It can easily be applied even by less experienced operators, and its results are sustainable beyond the scope of a clinical study.

Supplementary material

Supplementary material is available at *Europace* online.

Authorship contribution

D.R.M.: conceptualization (lead), review, and editing. A.M.d.C.: conceptualization (supporting) and data collection. E.A.R.A.-M.: data analysis. C.L.R.: data collection (supporting). M.G.C.: data analysis (supporting). J.R.J.: review and editing. L.B.B.: review and editing. F.A.Y.: conceptualization (supporting) and editing. R.S.-B.: conceptualization (supporting) and editing. All authors read and approved the submitted version of the manuscript.

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Conflict of interest: D.R.M. and F.A.Y. have received honoraria for lectures and educational events from Medtronic. All remaining authors have declared no conflicts of interest.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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