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## Relationship between ablation index and myocardial biomarkers after radiofrequency catheter ablation for atrial fibrillation<sup>☆</sup>

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### ABSTRACT

**Background:** Further in-vivo evidence is needed to support the usefulness of ablation index (AI) in guiding atrial fibrillation (AF) ablation. We aimed at evaluating the relationship between AI and other lesion indicators and the release of myocardial-specific biomarkers following radiofrequency AF ablation. **Methods:** Forty-six patients underwent a first-time radiofrequency AF ablation and were prospectively enrolled in this study. Pulmonary vein isolation was performed by six experienced electrophysiologists with a point-by-point approach, guided by strict Visitag criteria and consistent AI target values. Myocardial-specific biomarkers troponin T and creatine kinase myocardial band were measured after 6 (TnT6 and CKMB6) and 20 h (TnT20 and CKMB20) following sheath removal. Ablation duration, impedance drop (ID), force-time integral (FTI) and AI were registered automatically and analyzed offline. **Results:** TnT release was  $985 \pm 495$  ng/L and  $1038 \pm 461$  ng/L ( $p = ns$ ) while CKMB release was  $7.3 \pm 2.7$   $\mu$ g/L and  $6.5 \pm 2.1$   $\mu$ g/L ( $p < 0.001$ ) at 6 and 20 h respectively. Ablation duration, ID, FTI and AI were all significantly correlated with the release of myocardial-specific biomarkers both at 6 and 20 h. Ablation index showed the highest degree of correlation with TnT6, TnT20, CKMB6 and CKMB20 (Pearson's R 0.69, 0.69, 0.61, 0.64 respectively,  $p < 0.001$ ). Multiple regression analysis demonstrated that AI had the strongest association with TnT6, TnT20, CKMB6 and CKMB20 ( $\beta$  0.43,  $\beta$  0.71,  $\beta$  0.44 and  $\beta$  0.43 respectively).

**Conclusion:** Ablation index appears as the strongest lesion indicator as measured by the release of myocardial-specific biomarkers following radiofrequency catheter ablation for AF.

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## 1. Introduction

Radiofrequency (RF) catheter ablation aiming at electrical pulmonary vein (PV) isolation is an established treatment option for symptomatic drug-refractory atrial fibrillation (AF). Despite more than 20 years of scientific and technological advances, AF recurrence rates are significant, affecting up to 50% of patients after a single procedure [1–4]. Reconnection of one or several PVs can be

demonstrated in most patients experiencing AF recurrence. This is probably caused by inadequate lesions, reversible tissue injury and electrical reconduction [2]. Unpredictable lesion formation has been a major limiting factor for RF catheter ablation.

Contact force (CF) sensing catheters have been developed during the last decade. This technology allows accurate real-time measurement of catheter-tip-to-tissue contact, potentially leading to more predictable lesion formation and lower complication risk. Ablation index (AI) emerged as a novel lesion-quality indicator incorporating CF, RF duration and power in a weighted formula (Fig. 1). Experimental studies in animals showed good correlation between AI and lesion size [5,6]. However, evidence from randomized trials is lacking and there is need for further data to support the routine use of this indicator during RF catheter ablation for AF.

In this in-vivo model, we sought to analyze the relationship between several lesion indicators, including AI, and the release of myocardial-specific biomarkers following RF ablation for AF.

**Abbreviations:** AF, Atrial fibrillation; AI, Ablation index; CF, Contact force; CKMB, Creatine kinase myocardial band; FTI, Force-time integral; ID, Impedance drop; PV, Pulmonary vein; RF, Radiofrequency; TnT, Troponin T.

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$$AI = \left( k * \int_0^T CF^a(t) P^b(t) dt \right)^c$$

**Fig. 1.** Ablation index formula

Patented formula for calculation of ablation index. AI = ablation index, CF = contact force, P = power, t = time. Formula courtesy of Biosense Webster.

## 2. Methods

In this prospective, single-center, observational study, we enrolled 46 patients who underwent their first-time RF ablation procedure for symptomatic, drug-refractory AF. We included only first-time procedures to limit the effect of pre-existing left atrial scar on the release of biomarkers. Other exclusion criteria were previous myocardial infarction within three months, previous heart surgery or ablation, and severe kidney failure > stage 3 CKD.

Ablation procedures were performed in a fasting state using mild sedation or under general anesthesia. Intracardiac thrombi were excluded by transoesophageal echocardiography prior to the procedure. All patients were appropriately anticoagulated with either direct oral anticoagulants or vitamin K antagonist for at least 4 weeks prior to ablation; anticoagulation was upheld the morning of the procedure and reconvened during the same evening.

Six different electrophysiologists performed the procedures unaware of the patients' inclusion in the present study. Double transseptal puncture was performed in all patients. A steerable sheath (Agilis NxT™, Abbott, USA) was used in all patients to improve support for the ablation catheter. A 3.5-mm fully irrigated CF-sensing RF ablation catheter (Navistar Thermocool Smart-touch®, Biosense Webster, USA) was employed in all procedures. Catheter visualization was provided by standard fluoroscopy combined with a dedicated 3D navigation system (Carto3® ver. 7, Biosense Webster, USA).

Radiofrequency energy was delivered with a point-by-point approach aimed at the PV antrum in order to obtain encirclement of the PVs and bidirectional PV isolation. All operators aimed at an interlesion distance <6 mm according to the CLOSE protocol [7]. Radiofrequency energy was delivered from a Smart Ablate™ RF generator (Stockert GmbH, Germany), power output was left to the operator's discretion between 30 and 40 W, while irrigation flow was maintained at 2–25 ml/min. As suggested in previous studies, ablation was titrated to a target AI of 500–550 on the anterior wall and 380–400 on the posterior wall [7–10]. Lesions were visualized in the Carto3 system only after fulfilling pre-specified Visitag criteria (maximum distance 3 mm for a minimum of 3 s, maximum 25% variation force-over-time with a minimum CF of 3 g). Patients who still presented AF after complete ablation lines encircling the PVs underwent electrical cardioversion in order to verify bidirectional PV isolation. Patients with a clinical documentation of typical atrial flutter received additional cavotricuspid isthmus ablation with the endpoint of bidirectional conduction block.

Blood samples were drawn from the antecubital vein on hospital admission, then post-procedurally, 6 and 20 h from sheaths withdrawal. High-sensitive troponin T (TnT6 and TnT20 respectively) and creatine kinase myocardial band (CKMB6 and CKMB20 respectively) were measured using the Cobas e602 analyzer (Roche Diagnostics, Switzerland). Patients were monitored for 24 h following the ablation procedures before being discharged.

Procedural data were exported from the Carto3 system to a dedicated study database and analyzed offline. In particular, we retrieved ablation time, CF, maximum power, maximum temperature, impedance drop (ID), force-time integral (FTI) and AI for each lesion fulfilling the Visitag criteria. Duration of total delivered

energy was retrieved from the RF generator. Since release of myocardial biomarkers reflects the total amount of myocardial injury, our independent variables consisted of the total ablation duration, total ID, total FTI and total AI.

The electronic patient files were consulted for collection of baseline information. Personal data underwent anonymization using our institution's encryption software. All patients provided informed consent upon inclusion in this study.

The project was approved by the Regional Ethics Committee and it was conducted in accordance with the requirements stated in the Helsinki Declaration. The data underlying this article may be shared on reasonable request to the corresponding author.

## 3. Statistical analysis

Continuous variables are presented as means ± standard deviations while categorical variables as counts (frequencies). Independent and paired sample T-tests were used when appropriate to evaluate significant differences. ANOVA analysis of variance was used to test differences in continuous variables among several groups. Bivariate correlation was calculated using the Pearson's R coefficient. In order to assess individual contribution to the dependent variables, univariate and multiple regression analysis were employed after ensuring that assumptions were not violated. A statistical difference <0.05 was considered as significant. SPSS Statistics for Windows version 17.0 (SPSS Inc., USA, released 2008) was employed for data analysis.

## 4. Results

Forty-six patients (34 males, 74%) underwent successful RF ablation with the endpoint of bidirectional PV isolation. Demographic and baseline characteristics are presented in Table 1. Of note, 7 patients (15%) had mildly impaired left ventricular function but were in a well-compensated clinical condition. Nineteen patients (41%) suffered from persistent AF but received only ablation aimed at PV isolation. Eight patients (17%) with clinically documented counterclockwise atrial flutter received additional cavotricuspid isthmus ablation. General anesthesia was required in 2 patients.

Mean ablation time was 2327 ± 649 s among which 2258 ± 617 s (97.0%) fulfilled Visitag criteria and were registered as lesions by the Carto3 system. Mean lesion duration was 20.0 ± 3.5 s, mean CF was 15.9 ± 4.2 g, mean maximum power was 35.3 ± 1.5 W, and mean maximum catheter tip temperature was 35.3 ± 3.0 °C. The proportion of ablation time that fulfilled Visitag criteria was not different between the operators (ANOVA p = 0.36). On the other side, significant differences in average CF were found between the different operators (ANOVA p < 0.001, Fig. 2).

Troponin T increased significantly from baseline to 6 and 20 h after the procedure to a mean value of 985 ± 495 ng/L and 1038 ± 461 ng/L, respectively. The absolute increase between TnT6 and TnT20 was numerically marginal and not statistically significant (p = 0.23).

Creatine kinase myocardial band increased significantly from baseline to 6 h after the procedure to a mean value of 7.3 ± 2.7 µg/L followed by a small, albeit significant decrease after 20 h (6.5 ± 2.1 µg/L; p < 0.001). Biomarkers release did not differ significantly between the subgroups paroxysmal AF, persistent AF, AF only and combined AF + AFL (Table 2).

Adjusting release of cardiac biomarkers for ablation time revealed differences between different operators (ANOVA p = 0.072 for TnT6, p = 0.006 for TnT20, p = 0.026 for CKMB6 and p = 0.009 for CKMB20). Differences in time-adjusted biomarkers release reflected to some extent differences in mean CF between operators

**Table 1**  
Baseline characteristics.

<b>Total patient population</b>	46
<b>Gender male N (%)</b>	34 (74%)
<b>Age (years)</b>	61.2 ± 10.6
<b>Paroxysmal AF (%)</b>	27 (59%)
<b>Documented typical atrial flutter (%)</b>	8 (17%)
<b>Body mass index (%)</b>	27.7 ± 4.8
<b>Body surface area (m<sup>2</sup>)</b>	2.1 ± 0.2
<b>Indexed left atrial volume (ml/m<sup>2</sup>)</b>	48.8 ± 12.4
<b>Left ventricle ejection fraction (%)</b>	53 ± 5
<b>Baseline serum creatinine (μmol/L)</b>	84.2 ± 16.5 (ref 45–90)
<b>Baseline estimated GFR (ml/L/1.73m<sup>2</sup>)</b>	81.3 ± 14.8 (ref >60)
<b>Baseline troponin T (ng/L)</b>	8.1 ± 3.2 (ref <14)
<b>Baseline creatine kinase myocardial band (μg/L)</b>	2.4 ± 1.2 (ref <5)
<b>Baseline pro-BNP (ng/L)</b>	386.7 ± 421.1 (ref <300)

Baseline characteristics presented either as means ± standard deviations or as counts (percentages). Laboratory analyses are presented together with relevant reference range. AF: atrial fibrillation, GFR: glomerular filtration rate, BNP: brain natriuretic peptide.

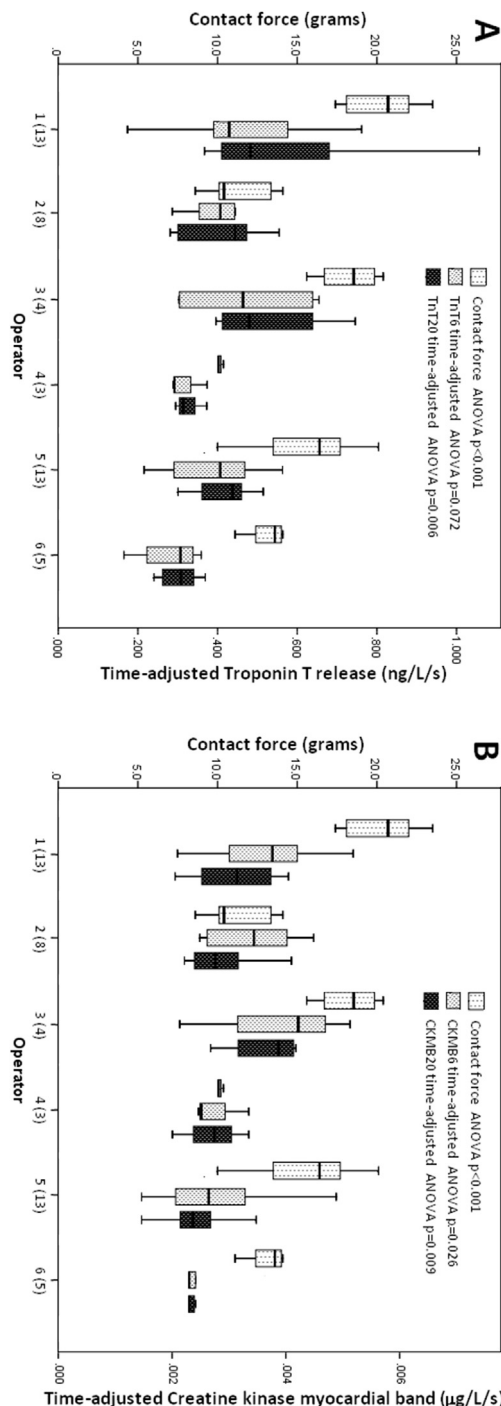
(Fig. 2). Time-adjusted biomarkers release showed some degree of correlation with CF (TnT6 R 0.23 p = 0.12, TnT20 R 0.52 p < 0.01, CKMB6 R 0.38 p = 0.01, CKMB20 R 0.45 p < 0.01), but not with indexed left atrial volume (TnT6 R 0.19 p = 0.20, TnT20 R 0.19 p = 0.22, CKMB6 R -0.01 p = 0.96, CKMB20 R 0.06 p = 0.68).

Total ablation time, total ID, total FTI and total AI were significantly correlated with TnT6, TnT20, CKMB6 and CKMB20. AI showed the highest correlation coefficients for all the dependent variables. Scatter-plots, correlation coefficients and significance levels are presented in Fig. 3. Univariate regression analysis is presented in Table 3.

A preliminary assessment revealed that FTI and AI were significantly correlated with each other (Pearson's R = 0.89) thus violating the multicollinearity assumption for multiple linear regression. In order to circumvent this issue, two regression models were built for each dependent variable including ablation duration, ID and FTI in the first, and ablation duration, ID and AI in the second (Table 4). Models including AI had consistently a higher adjusted R<sup>2</sup> value, suggesting that the inclusion of AI explained higher levels of variance for the dependent variables. Additionally, standardized β coefficients were consistently higher for AI than for all other independent variables, although only a trend towards statistical significance was observed for CKMB6 and CKMB20 (p = 0.069 and p = 0.066 respectively).

## 5. Discussion

In this in-vivo AF ablation model, surrogate lesion indicators (ID, FTI, AI) as well as total ablation duration correlated with the actual myocardial injury as measured by myocardial-specific biomarkers. The different statistical analyses performed in this study point in the same direction and suggest AI as the strongest lesion indicator. When adjusted for ablation duration, release of biomarkers varied between different operators, reflecting to some extent differences in mean CF.



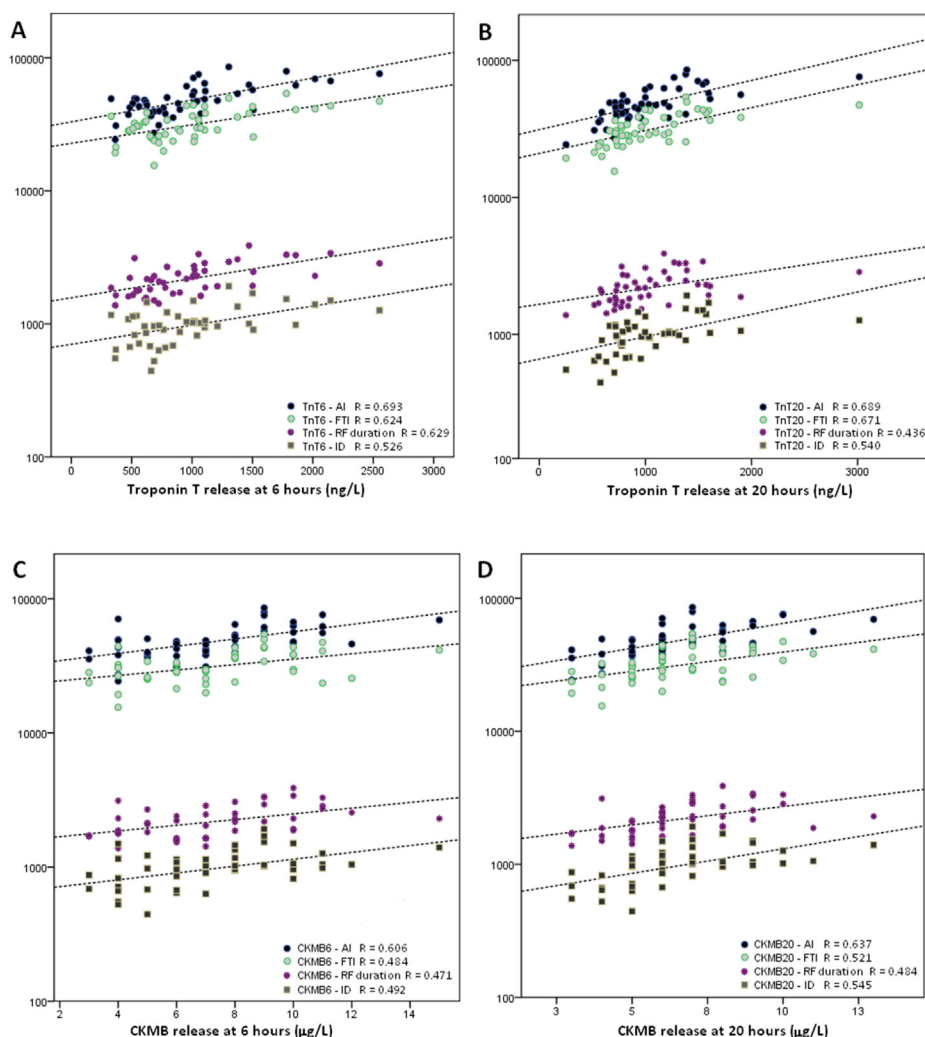
**Fig. 2.** Distribution of contact force and time-adjusted release of myocardial specific biomarkers between different operators.

Boxplot showing median and dispersion of CF (y axis) and time-adjusted release of biomarkers (z axis) between the six different operators (x axis). Number of procedures per operator is given in brackets. Panel A includes time-adjusted TnT release while panel B includes time-adjusted CKMB release after 6 and 20 h from the ablation procedure. ANOVA test between groups showed differences p < 0.001 for CF, p = 0.072 for TnT6, p = 0.006 for TnT20, p = 0.026 for CKMB6 and p = 0.009 for CKMB20. Differences in CF reflected to a certain degree differences in time-adjusted release of biomarkers. CKMB = creatine kinase myocardial band, CF = contact force, TnT = troponin T.

**Table 2**  
Release of myocardial biomarkers between subgroups.

	Paroxysmal AF (n = 27)	Persistent AF (n = 19)	Sig.	AF only (n = 38)	AF + AFL (n = 8)	Sig.
<b>TnT 6 h (ng/L)</b>	986 ± 501	984 ± 500	0.986	934 ± 473	1228 ± 555	0.128
<b>TnT 20 h (ng/L)</b>	1077 ± 541	981 ± 321	0.490	1026 ± 486	1094 ± 336	0.709
<b>CKMB 6 h (µg/L)</b>	7.5 ± 2.3	7.1 ± 3.0	0.559	7.1 ± 2.7	8.5 ± 1.9	0.167
<b>CKMB 20 h (µg/L)</b>	6.5 ± 2.0	6.6 ± 2.4	0.882	6.3 ± 2.2	7.4 ± 1.8	0.220

Release of biomarkers between subgroups. AF = atrial fibrillation, AFL = atrial flutter, CKMB = creatine kinase myocardial band, TnT = troponin T.



**Fig. 3.** Correlation between ablation duration, impedance drop, force-time-integral and ablation index and the release of myocardial specific biomarkers. Scatter-plot showing spatial dispersion, best-fit line and Pearson's R coefficient for TnT at 6 h (panel A), TnT at 20 h (panel B), CKMB at 6 h (panel C), CKMB at 20 h (panel D). In order to accommodate parameters with different size, a logarithmic scale was employed (y axis). All correlations were significant at  $p < 0.001$  level. Units of measure in y axis: s for RF duration, ohm for ID, g\*s for FTI, unspecified unit for AI. AI = ablation index, CKMB = creatine kinase myocardial band, CF = contact force, FTI = force-time integral, ID = impedance drop, RF = radiofrequency, TnT = troponin T.

**- Assessment of lesion quality, a pitfall for durable PV isolation**

Reconnection of one or more PVs is common following catheter ablation, and it is believed to be the pivotal mechanism leading to AF recurrence [1–4]. Inadequate lesions during the first ablation procedure may create local oedema that prevents transmural necrosis; despite acute conduction block the injured tissue may regain conduction after resolution of inflammation. Interlesion distance recently emerged as an additional critical variable for avoiding isolation gaps and PV reconnection. Although the present study followed the CLOSE protocol, considerations around interlesion distance were out of the scope of this work [7].

Surrogate parameters have been employed since the early days of catheter ablation era to monitor lesion development. However, parameters like electrogram amplitude, ID and tactile feedback proved to be poor predictors and associated with high intra- and interoperator variability. In the last decade, the advent of real-time CF monitoring revolutionized the field of RF catheter ablation. Convincing evidence both from experimental and clinical studies demonstrated that CF is a key factor for lesion formation [8–12]. Contact force measures have been validated in numerous animal experiments, showing consistently that higher degrees of CF resulted in larger and deeper lesions [11]. With the availability of this information, ablation practice could shift from a fixed-power,

**Table 3**  
Univariate regression analysis.

TnT 6 h	$\beta$	Sig.
RF duration	0.629	<0.001
ID	0.526	<0.001
FTI	0.624	<0.001
AI	0.693	<0.001
TnT 20 h	$\beta$	Sig.
RF duration	0.436	0.002
ID	0.540	<0.001
FTI	0.671	<0.001
AI	0.689	<0.001
CKMB 6 h	$\beta$	Sig.
RF duration	0.471	0.001
ID	0.492	0.001
FTI	0.484	0.001
AI	0.606	<0.001
CKMB 20 h	$\beta$	Sig.
RF duration	0.484	0.001
ID	0.545	<0.001
FTI	0.521	<0.001
AI	0.637	<0.001

Univariate regression analysis for each dependent variable. Ablation index showed consistently the highest  $\beta$  coefficient. N = 46 for all models. AI = ablation index, CKMB = creatine kinase myocardial band, ID = impedance drop, FTI = force-time-integral, RF = radiofrequency, TnT = troponin T.

fixed-duration to one in which power, CF and duration could be titrated to achieve a desired effect.

FTI and AI are lesion indicators that were designed to outclass their predecessors in predicting ablation effect. FTI is the mere product of CF and ablation duration. The TOCCATA study was the

first to link higher FTI values to improved clinical outcomes [3]. Oppositely, ablation resulting in low FTI was found to be associated with isolation gaps and delayed PV reconnections [4].

AI is a further evolution incorporating CF, ablation duration and power in a weighted logarithmic formula. Experimental models showed robust correlation between AI and lesion size, superior to the one with FTI [5,6]. Multiple observational and clinical studies support the routine use of AI to guide AF ablation [8,9,12,13]. However, ultimate data from randomized controlled trials is lacking.

**- Troponin T and CKMB as markers of myocardial injury following AF ablation**

Cardiac biomarkers such as TnT and CKMB are intracellular cardiomyocyte proteins, widely used in the diagnostics of acute coronary syndrome [14]. Modern immunoassays for these biomarkers are highly sensitive, especially for TnT, and able to detect minimal changes. Given their additional tissue specificity and rapid release to the circulating blood, it is reasonable to regard TnT and CKMB release as direct measures of myocardial injury also following catheter ablation.

The relationship between surrogate lesion indicators and biomarkers release after catheter ablation is poorly studied. However, previous work investigated the association between ablation duration and biomarkers release with discordant results [15–19]. This incongruence is seen probably because other intraprocedural parameters than just ablation duration, are involved in the release of biomarkers. Moreover, external factors (time-dependency in release, myocardial fibrosis, heart failure, kidney function among others) may also affect biomarkers release and should be taken into account.

**Table 4**  
Multiple regression analysis.

TnT release at 6 h RF duration-ID-FTI Adjusted R <sup>2</sup> 0.487					TnT release at 6 h RF duration-ID-AI Adjusted R <sup>2</sup> 0.491				
	B	SE B	B	Sig.		B	SE B	$\beta$	Sig.
RF duration	0.317	0.095	0.416	<b>0.002</b>	RF duration	0.228	0.115	0.299	0.054
ID	0.122	0.265	0.078	0.647	ID	0.125	0.257	0.079	0.629
FTI	0.020	0.010	0.350	0.054	AI	0.015	0.007	0.425	<b>0.045</b>
TnT release at 20 h					TnT release at 20 h				
RF duration-ID-FTI Adjusted R <sup>2</sup> 0.424					RF duration-ID-AI Adjusted R <sup>2</sup> 0.442				
	B	SE B	B	Sig.		B	SE B	$\beta$	Sig.
RF duration	0.087	0.094	0.123	0.357	RF duration	-0.054	0.112	-0.076	0.635
ID	0.067	0.261	0.045	0.800	ID	0.057	0.251	0.039	0.821
FTI	0.031	0.010	0.573	<b>0.004</b>	AI	0.023	0.007	0.712	<b>0.002</b>
CKMB release at 6 h					CKMB release at 6 h				
RF duration-ID-FTI Adjusted R <sup>2</sup> 0.283					RF duration-ID-AI Adjusted R <sup>2</sup> 0.333				
	B	SE B	$\beta$	Sig.		B	SE B	$\beta$	Sig.
RF duration	0.001	0.001	0.290	0.055	RF duration	0.000	0.001	0.117	0.502
ID	0.002	0.002	0.271	0.179	ID	0.001	0.002	0.114	0.547
FTI	0.000	0.000	0.126	0.551	AI	0.000	0.000	0.439	0.069
CKMB release at 20 h					CKMB release at 20 h				
RF duration-ID-FTI Adjusted R <sup>2</sup> 0.335					RF duration-ID-AI Adjusted R <sup>2</sup> 0.382				
	B	SE B	$\beta$	Sig.		B	SE B	$\beta$	Sig.
RF duration	0.001	0.000	0.280	0.055	RF duration	0.000	0.001	0.111	0.508
ID	0.002	0.001	0.330	0.092	ID	0.001	0.001	0.177	0.331
FTI	0.000	0.000	0.123	0.545	AI	0.000	0.000	0.427	0.066

Multiple regression models for each dependent variable including ablation duration, impedance drop and force-time integral (left side) and including ablation duration, impedance drop and ablation index (right side). Unstandardized coefficient B, standard error (SE B), standardized coefficient  $\beta$  and significant level is given for each independent variable. Regression analysis shows consistently that adjusted R<sup>2</sup> values for models including ablation index were higher than for those including force-time integral. Additionally, standardized  $\beta$  coefficients for AI were consistently higher than for other independent variables. N = 46 for all models. AI = ablation index, CKMB = creatine kinase myocardial band, ID = impedance drop, FTI = force-time-integral, RF = radiofrequency, TnT = troponin T.

During this investigation, an effort was put to collect blood samples consistently at 6 and 20 h after ablation. Exclusion criteria were framed to prevent confounding from other clinical conditions such as previous ablation, heart surgery, recent myocardial infarction and severe kidney failure. No patient presented symptoms of acute coronary syndrome during the observational period. A strict ablation protocol was followed and 97.0% of ablation time fulfilled pre-specified Visitag criteria. Therefore, we may reasonably assume that the release of cardiac biomarkers observed in this study, directly reflects ablation effect.

The release of TnT and CKMB in our material is comparable to previous studies [15,16]. Troponin T release was flat and did not exhibit the typical variation usually seen after acute myocardial infarction. On the other side, the significant decrease in CKMB after 20 h can be explained by its more rapid decay in the circulation [14].

Yoshida et al. suggested that higher TnT release might predict better clinical outcomes after AF ablation [18]. The authors speculated that a higher TnT after ablation may be a marker of a healthier left atrium thus linking indirectly TnT release to improved clinical outcomes.

Similarly, Wynn et al. showed that an ablation effectiveness quotient consisting in the amount of TnT release adjusted for RF duration could predict arrhythmia recurrence [19]. Although clinical endpoints were not investigated in the present study, our findings suggest that higher release of biomarkers reflects higher RF duration, CF, FTI and AI rather than healthier left atria. As a matter of fact, no significant association was found between time-adjusted biomarkers and left atrial volume in our material.

#### - Ablation index: the new gold-standard indicator to monitor lesion development?

Seminal experimental work in animal models demonstrated that lesion depth could be accurately predicted by a parameter incorporating CF, power and time in a logarithmic formula [5]. In experimental conditions, correlation coefficient up to 0.87 was reported between lesion volume and AI [6]. Observational studies have later confirmed the importance of AI by correlating this parameter to ID, a widely used lesion indicator [13,20]. Furthermore, the use of AI has been linked to improved clinical outcomes after RF ablation [9–10]. A recent meta-analysis including 11 studies for a total of 2306 patients found that AI-guided PV isolation resulted in shorter procedural times, higher rate of first-pass PV isolation and most importantly lower incidence of AF recurrence compared to non-AI guided procedures [8]. However, it is noteworthy that studies included in this meta-analysis were neither randomized nor employed implantable loop-recorders to document arrhythmia-recurrences.

#### - Implications to clinical practice

The ultimate goal of AF ablation is to perform durable long-lasting PV isolation; in this regard, transmural lesions are crucial. Catheter-tip-to-tissue CF may vary significantly, being affected by operator, equipment (steerable sheaths) or patient-related (respiration, anatomy) factors, as demonstrated in this study. AI offers valuable information in predicting lesion quality and may also be useful for more standardized and consistent procedures.

In the present study we employed an in-vivo model to investigate the impact of different lesion indicators on the extent of myocardial damage. Our findings confirm and extend previous knowledge: AI outperformed other parameters in predicting lesion size as measured by the release of myocardial-specific biomarkers. Association between AI and TnT was consistently significant, while

we observed only a trend to statistical significance concerning CKMB. The reason for this inconsistency may be explained by the lower sensitivity of the CKMB assay (measuring  $\mu\text{g/L}$  rather than  $\text{ng/L}$  as for TnT) as well as its known thermolability and potentially lower circulating levels after RF ablation [21].

A multicenter randomized controlled trial comparing conventional CF-guided to AI-guided AF ablation is currently in the recruiting phase [22]. Until results from the latter are published, our findings add to the existing body of evidence and support the routine use of AI in assisting PV isolation.

#### - Limitations

This was a single-center investigation of a limited sample size. Although we enrolled only patients undergoing first-time AF ablation and an effort was made to account for left atrial indices, routine cardiac MRI was not performed, and we therefore cannot exclude preexisting left atrial fibrosis. Although our population had rather homogeneous kidney function, we cannot exclude that even small differences in renal clearance may have affected biomarkers measured in this study. Power output was left at the operator's discretion, potentially affecting our independent variables. However, a standard deviation of just  $\pm 1.5$  W in maximum power among all patients suggests only a negligible impact. Due to the lack of extended follow-up in this study, no inferences can be made with clinical outcomes.

#### 6. Conclusions

Ablation duration, ID, FTI and AI are directly correlated with the magnitude of myocardial injury as measured by the release of TnT and CKMB. AI appeared as the strongest lesion indicator: this study supports its routine use during RF ablation for AF.

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#### Declaration of competing interest

Authors declare no Conflict of Interests for this article.

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