Mapping and ablation of non-pulmonary vein drivers of persistent atrial fibrillation: Has a STAR been born?

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December 20, 2020

Abstract

While pulmonary vein isolation (PVI) remains the cornerstone for invasive treatment of atrial fibrillation (AF), patients with persistent AF still have a high rate of recurrence with this method. Stochastic Trajectory Analysis of Ranked signals (STAR) mapping uses data from multiple individual wavefronts during ongoing AF to identify local drivers of persistent AF. In this non-randomized study, STAR mapping and ablation showed significantly lower recurrence of atrial arrhythmias compared to a consecutive PVI-only cohort and a propensity-matched 'conventional ablation' cohort (consisting of PVI plus complex fractionated atrial electrogram ablation or linear ablation). This benefit was driven by a much lower rate of AF recurrence in the STAR (6.2%) cohort vs PVI-only (44%) or 'conventional' (40%) with no significant difference in atrial tachycardia recurrence. Additionally, AF termination rates during ablation were approximately three times higher in the STAR cohort. While the analysis is retrospective and not randomized, the STAR cohort was also the only cohort with complete cessation of anti-arrhythmic drugs at three months and Holter monitoring at 6 and 12 months post-ablation per protocol. While STAR mapping appears to be a very promising new tool for treating persistent AF, history predicts at least some regression to the mean when future randomized comparisons are made. The authors have planned a multicenter randomized trial of PVI plus STAR mapping vs PVI-only for persistent AF. The global community of electrophysiologists and patients with AF eagerly awaits the results.

Mapping and ablation of non-pulmonary vein drivers of persistent atrial fibrillation: Has a STAR been born?

Short Title: STAR mapping for persistent atrial fibrillation

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Disclosures: Jay Montgomery has received consulting fees from Medtronic.

Funding: None

Abstract:

While pulmonary vein isolation (PVI) remains the cornerstone for invasive treatment of atrial fibrillation (AF), patients with persistent AF still have a high rate of recurrence with this method. Stochastic Trajectory Analysis of Ranked signals (STAR) mapping uses data from multiple individual wavefronts during ongoing AF to identify local drivers of persistent AF. In this non-randomized study, STAR mapping and ablation showed significantly lower recurrence of atrial arrhythmias compared to a consecutive PVI-only cohort and a propensity-matched 'conventional ablation' cohort (consisting of PVI plus complex fractionated atrial electrogram ablation or linear ablation). This benefit was driven by a much lower rate of AF recurrence in the STAR (6.2%) cohort vs PVI-only (44%) or 'conventional' (40%) with no significant difference in atrial tachycardia recurrence. Additionally, AF termination rates during ablation were approximately three times higher in the STAR cohort. While the analysis is retrospective and not randomized, the STAR cohort was also the only cohort with complete cessation of anti-arrhythmic drugs at three months and Holter monitoring at 6 and 12 months post-ablation per protocol. While STAR mapping appears to be a very promising new tool for treating persistent AF, history predicts at least some regression to the mean when future randomized comparisons are made. The authors have planned a multicenter randomized trial of PVI plus STAR mapping vs PVI-only for persistent AF. The global community of electrophysiologists and patients with AF eagerly awaits the results.

Keywords:

Multipolar mapping, electroanatomic mapping, atrial fibrillation, persistent atrial fibrillation, atrial fibrillation ablation

While pulmonary vein isolation (PVI) remains the cornerstone for invasive treatment of atrial fibrillation (AF), patients with persistent AF still have a high rate of recurrence with this method.[1, 2] Over the last two decades, a multitude of strategies beyond PVI (such as ablation of lines connecting two unexcitable structures, complex fractionated atrial electrograms ablation, or rotor ablation) have shown promise as adjunctive treatments for patients with persistent or longstanding persistent AF.[3-6] However, most of these initially-promising strategies have failed to show benefit in multicenter randomized trials.[1, 7] Furthermore, methods that have shown additional benefit over PVI in multicenter RCTs may raise the risk of procedural or post-procedure complications (as in the case of hybrid surgical ablation or left atrial appendage isolation) or require a different skillset while still leaving a relatively large proportion of patients with recurrence (vein of Marshall ethanol injection).[8-12]

It is in this setting that Honarbakhsh et al present their most recent retrospective analysis of a novel technique for mapping and ablation of persistent AF substrate, referred to as Stochastic Trajectory Analysis of Ranked signals (STAR) mapping.(cite the paper you are publishing along with the editorial) In brief, STAR mapping uses data from multiple individual wavefront trajectories during ongoing AF in search of regions of the atrium that usually precede all nearby areas (thereby acting as the local source). Areas that activate earliest most often are targeted for ablation first, and no further sites are targeted if ablation terminates AF. The computation is carried out via a script in Matlab (Mathworks, MA, USA) written by one of the authors. In this study, data collection was performed using either whole-chamber basket catheters or standard multipolar catheters.[13]

This study consists of two separate contemporary comparisons: STAR mapping compared to a propensity-matched 'conventional ablation' cohort and STAR mapping compared to consecutive patients undergoing PVI-only. In the first analysis, 65 consecutive patients who underwent STAR mapping with PVI were compared to a propensity-matched cohort who had 'conventional ablation' (PVI plus CFAE and/or linear ablation) from the same operators during the same time period. The second analysis compared the same STAR patients to 50 consecutive patients who underwent PVI-only for persistent AF. All three cohorts had

an average duration of ongoing AF > 12 months, though no patient had been in continuous AF > 24 months (per study protocol). The authors state that a majority of patients had AF duration >12 months.

The principal finding was a significant decrease in AF/atrial tachycardia (AT) recurrence in the STAR group (20.0%) compared to either the PVI-only group (50.0%) or the 'conventional' group (50.8%) driven by a reduction in AF, but not AT, at [?]20 months. Only 6.2% of patients in the STAR group had documented AF recurrence, while 13.8% recurred with AT compared to 40% AF and 10.8% AT recurrence in the 'conventional' group and 44% AF and 6% AT recurrence in the PVI-only cohort. AF termination rates during ablation were also significantly higher in the STAR cohort (69.2%) compared to the conventional ablation cohort (15.4%) or the PVI-only cohort (26.0%; p<0.001 for both comparisons). It is not clear how or why the rate of AF termination was higher in the PVI-only group than the conventional ablation group, but the overall numbers of AF terminations in these two groups was small, and these two groups were not matched in any way to one another. Therefore, this apparent discrepancy between the 'control' groups could be due to chance or selection bias.

Procedure time was not statistically different in the STAR, conventional, and PVI-only groups (225.4±65.6 min vs. 219.0±64.8 min vs. 208.5±59.4min; p=NS for both comparisons), though the total RF time was greater in the STAR group than the PVI-only group. The fact that the STAR method appeared to add only 17 minutes to the procedure time over PVI seems like a reasonable concession for a method that appears to improve outcomes. However, the fact that the 'conventional' ablation group procedure time was only 11 minutes longer than the PVI-only group suggests that this group did not, in general, have extensive substrate modification (seven had only cavotricuspid isthmus ablation as the only ablation beyond PVI).

The overall methods of the paper are somewhat complex given two separate comparisons with different types and degrees of matching between the groups. Additionally, the analysis is retrospective in nature, and it cannot be known why a patient would receive STAR mapping, 'conventional ablation,' or PVI-only. Therefore, this study is useful for hypothesis generation, but it does not prove causation with regard to differential outcomes as the groups are very likely different. That being said, the methods (other than assignment to groups) would likely favor the STAR group having *more complete* detection of clinically-silent recurrence as this was the only group with mandated rhythm monitoring (Holter at 6 and 12 months). The STAR cohort was also the only group in whom all AADs were stopped at 3 months post-ablation per protocol.

There is potentially a lot to like about the STAR method as described. The overall idea behind it (identify sites that repeatedly seem to activate prior to all nearby sites) seems more intuitive to the proceduralist and takes less time than, for example, focal impulse and rotor modulation as initially described.[5] While this technique seems somewhat similar in concept to *non* -invasive AF mapping that has been described previously, the present study seemed to show greater likelihood of AF termination when ablating AF drivers in those with AF lasting longer than 12 months and may not be associated with the same high rates of post-ablation AT.[14, 15]The exceptionally low rate of AF (rather than AT) recurrence (6.2%) in the STAR group provides cause for hope that this method is effectively targeting the sources of initiation and perpetuation of persistent AF. For comparison, the three arms of the STAR AF 2 trial (PVI-only, PVI plus lines, PVI plus CFAE) which enrolled patients with perhaps more advanced AF (lasting up to 3 years with left atrial size 4.4 cm as opposed to 3.8 cm in the current study) had AF recurrence rates of 41-59% at 18 months.[1] Providing at least a small dose of reality to the results of the current study, the 13.8% rate of AT recurrence with STAR mapping seems generally in-line with the 11-14% seen across the three arms of the STAR AF 2 trial.

Again, this is not a randomized study, and as such, assignment of causation is hazardous. While it is certainly possible that STAR mapping is much more effective than PVI alone or 'conventional ablation' as defined in this study for persistent AF, that would mean that this method is likely more successful than any prior endocardial method that has been tested in randomized trials for persistent AF. While that is very possible, and may even be likely, history predicts at least some regression to the mean in a randomized, multicenter evaluation.

Looking more generally to the horizon of AF treatment, we should anticipate therapies to improve the effectiveness and safety of our lesions (electroporation), to ablate tissue previously unreachable (ethanol injection into the vein of Marshall), and, perhaps, to identify ongoing non-pulmonary vein drivers of AF (STAR mapping). While we can hope that this is a breakthrough, the field of persistent AF ablation is littered with abandoned methods (beyond PVI) that have not been borne out in randomized studies. The authors have planned a multicenter randomized trial of PVI plus STAR vs PVI-only. The global community of electrophysiologists and patients with AF eagerly awaits the results.

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