REVIEW

by Prof. Tchavdar Nikolov Shalganov, MD, PhD
Department of Invasive Electrophysiology
Clinic of Cardiology
National Heart Hospital – Sofia

Review of a dissertation submitted for the award of the educational and scientific degree "**Doctor**" in Professional field 7.1. Medicine, Doctoral Programme "Cardiology"

Dissertation author: Dr. Krasimir Rosenov Dzhinsov, external doctoral candidate (independent training) at the Clinic of Cardiology, Acibadem City Clinic University Hospital Tokuda EAD

Dissertation title: "Significance of Radiofrequency Lesion Tagging and Their Characteristics in Pulmonary Vein Isolation in Patients with Atrial Fibrillation"

Scientific supervisor: Prof. Vassil Borislavov Traykov, MD, PhD
Clinic of Cardiology, Acibadem City Clinic University Hospital Tokuda EAD

This review has been prepared on the basis of Order No. 15-01-448#2/22.12.2025 of the Executive Director and the Procurator of Acibadem City Clinic University Hospital Tokuda EAD – Sofia, in accordance with the Act on the Development of the Academic Staff in the Republic of Bulgaria, its Implementing Regulations, and the Regulations for the Development of the Academic Staff of ACC UH Tokuda.

I declare that I have no joint scientific projects or publications on the topic of the dissertation with Dr. Krasimir Dzhinsov.

The submitted set of materials on electronic media complies with the procedures for obtaining the educational and scientific degree "Doctor" at ACC UH Tokuda EAD in accordance with the statutory requirements and includes:

- an application to the head of the scientific organization to initiate the procedure for dissertation defense;
- a Europass curriculum vitae signed by the doctoral candidate;
- a notarized copy of the higher education diploma;
- orders for enrollment in and deregistration from the doctoral program with the right to defense;
- an order for holding an examination from the individual plan and the relevant protocol for a passed examination or doctoral minimum in the specialty;
- minutes from the unit collegium for preliminary discussion of the dissertation and decisions to open the public defense procedure and appoint the scientific jury;
- the dissertation manuscript;
- an abstract;
- a list of scientific publications on the topic of the dissertation;
- copies of the scientific publications;
- a list of participations in scientific forums;
- a list of identified citations;
- a declaration of originality and authenticity of the submitted documents;
- other documents related to the course of the procedure;
- a report on compliance with the minimum national requirements.

The doctoral candidate has submitted three publications.

Brief Biographical Data

Dr. Krasimir Dzhinsov graduated in Medicine from the Medical University of Plovdiv in 2012. He obtained his specialty in Cardiology in 2017. He holds numerous certificates of professional qualification and licensure, the most significant of which are expert-level certificates in cardiac pacing and electrophysiology, a full certificate in electrophysiology from the European Heart Rhythm Association, and a DAS-CAM diploma from Maastricht University, the Netherlands. He has worked at the National Cardiology Hospital in Sofia and at St. George University Hospital in Plovdiv, where he headed the Invasive Electrophysiology and Cardiac Pacing Unit within the Department of Invasive Cardiology. Since 2021, he has been an assistant at the Medical Simulation Training Center of the Faculty of Medicine at the Medical University of Plovdiv. He holds a Master's degree in Health Management. He has participated in numerous scientific events. He is Chairman of ACEB, a member of BSC, a member of the ESC, and a member of professional associations within the ESC (EHRA, ACVC, EAPCI).

Relevance of the topic

Atrial fibrillation is the most widespread arrhythmia, negatively affecting quality of life, potentially leading to severe long-term health consequences, and consuming a substantial share of healthcare resources due to its recurrent or chronic nature. The most effective rhythm control strategy in atrial fibrillation is pulmonary vein isolation. In Bulgaria, this procedure is still predominantly performed as radiofrequency catheter ablation.

Achieving durable pulmonary vein isolation is of particular importance for long-term outcomes, including quality of life. Regardless of the technology used (energy source, three-dimensional mapping and navigation system, ablation protocol, etc.), mid-term recurrence rates range from approximately 5% to nearly 50%, depending on study design (randomized vs. observational) and study setting (leading vs. non-leading centers). The main cause of recurrence is reconnection to/from the pulmonary veins. One accessible approach to reducing reconnection rates is the application of a standardized ablation protocol that objectively accounts for parameters related to potential lesion transmurality and continuity of the ablation line. A universal standardized protocol does not exist; available protocols are limited to certain three-dimensional systems and specific types of ablation catheters, which are still relatively rarely used in Bulgaria. The possibility of applying a protocol with automatic lesion tagging based on real-time biophysical changes when using ablation catheters that do not measure contact force has not been studied to date. With regard to quality of life, it has been proven to improve after atrial fibrillation ablation; however, a universal method for assessing this change is lacking. Combining a generic quality-of-life questionnaire with an arrhythmia-specific questionnaire represents a hybrid approach that may provide a more comprehensive assessment.

Therefore, the dissertation topic addresses a current and insufficiently studied problem in cardiology. The author aims to compare procedural and clinical success, procedural characteristics, and changes in quality of life between automatic and manual lesion tagging during pulmonary vein isolation using non-contact-force sensing catheters.

Structure and content of the dissertation

The submitted dissertation consists of 192 standard pages and is structured in accordance with the requirements: literature review – 40 pages; aims, objectives, material and methods – 23 pages; results – 56 pages; discussion of results and methodological limitations – 22 pages; conclusions, contributions, and bibliography containing 336 references, 7 of

which are in Cyrillic. Thirty-seven of the cited references are from the last five years. The work is illustrated with 44 figures and 28 tables presenting the author's original results.

Literature review

The literature review is clearly and competently written and demonstrates the author's broad knowledge of the subject matter. The various methods for achieving durable isolation, as well as for avoiding and detecting gaps in ablation lines, are well described. Key data from previous studies on methods for assessing isolation and ablation line continuity, as well as changes in quality of life after atrial fibrillation ablation, are systematically presented. The review concludes with a summary that logically leads to the formulation of the study aim.

Aims and objectives

The aims and objectives of the study are clearly, concisely, and precisely formulated.

Material and methods

The primary scientific material includes 131 patients undergoing first-time catheter pulmonary vein isolation in three centers: St. George University Hospital, Plovdiv (n = 33); National Heart Hospital, Sofia (n = 48); Acibadem City Clinic University Hospital Tokuda, Sofia (n = 50). Automatic lesion tagging was performed in all patients. The patients were divided into two groups: 48 patients with additional manual tagging, with automatic tagging hidden during the procedure; 83 patients with automatic tagging only, visible during the procedure.

Inclusion criteria were simple, while exclusion criteria were detailed and excluded patients with severe cardiac or comorbid conditions.

Procedures were performed using the same three-dimensional mapping system but with two types of ablation catheters differing in tip cooling and energy delivery. Automatic tagging parameters and values recommended by the system manufacturer were used. High-quality original material was used for illustration. Technical descriptions are detailed. Dedicated software was developed and used for lesion characteristic calculations and visualizations. Quality of life was assessed using the EuroQol EQ-5D-5L questionnaire with its visual analogue scale, as well as the modified EHRA score (mEHRA) for symptom severity in atrial fibrillation. Endpoints for success were clearly and unambiguously defined.

Statistical methods are described in great detail and are appropriate for the material and study objectives.

Results

The patient population is typical in terms of demographic and clinical characteristics. Distribution of most parameters within the two groups is comparable.

Numerous exploratory analyses of multiple variables and their interrelationships were performed. Identified associations were weak, although statistically significant, which is important in avoiding future repetition of studies on weak correlations with limited clinical relevance.

Automatic tagging detected gaps in the ablation line significantly more often, without affecting acute reconnection or recurrence during follow-up. With a mean follow-up of nearly 40 months, no significant difference in recurrence-free survival was observed. During repeat ablation, no association was found between the presence of gaps and reconnection. A particularly important positive finding is the significant reduction in radiofrequency and overall procedural time.

Another very important confirmatory finding is the marked and significant improvement in quality of life according to both questionnaires. In EQ-5D-5L, substantial

and highly significant improvement was observed in all five dimensions, as well as in the visual analogue scale and EQ index. Similarly, the modified EHRA score improved, with nearly 78% of patients becoming asymptomatic, and only one patient continuing to experience moderate or severe limiting symptoms compared to 33% at baseline. Follow-up for quality of life covered over 80% of patients, which is a notable achievement given the mean follow-up duration.

Another important finding is the procedural success at 12 and 24 months (77% and 65%, respectively), consistent with outcomes reported in other real-world studies, indicating that procedural quality in the three centers is fully comparable to that of other centers in Europe and worldwide.

Discussion

The discussion compares the obtained results with those reported by other authors. The importance of a comprehensive approach to atrial fibrillation management, targeting all modifiable risk factors for recurrence, is rightly emphasized. Interpretation of the statistically significant associations with thyroid disease and mitral regurgitation is cautious and appropriate, acknowledging the small number of patients and wide confidence intervals, and the need for further confirmation. Of particular practical importance is the equalization of clinical success after repeat ablation in patients with thyroid dysfunction, justifying a lower threshold for re-ablation in case of recurrence.

The importance of automatic tagging for objective assessment of widely available lesion characteristics, regardless of catheter type, and for avoiding unnecessary repeat applications—leading to reduced procedural and cumulative radiofrequency time and consequently reduced radiation exposure—is correctly highlighted.

Regarding quality of life, the author appropriately emphasizes that age and biological sex should not be decisive factors in ablation decisions, as improvement is independent of these parameters. The suggested explanation for quality-of-life improvement in mitral regurgitation—reverse remodeling and reduction of functional regurgitation—is somewhat speculative due to lack of echocardiographic follow-up, but represents an interesting hypothesis for further investigation, particularly in atrial functional mitral regurgitation.

The author's commentary on binary recurrence assessment and quality of life is highly appropriate. In modern concepts of atrial fibrillation burden, reduction of burden rather than mere documentation of any recurrence is essential. Unfortunately, practical assessment of atrial fibrillation burden reduction requires significant resources, making it difficult to implement and fully justifies the choice of tracking methods in the present work.

The inclusion of a detailed section on methodological considerations and limitations is a strong positive aspect.

Conclusions and contributions

The seven conclusions are clearly formulated and directly derived from the analyzed data.

Summary of contributions: (1) Systematic comparison of manual and automatic radiofrequency lesion tagging during pulmonary vein isolation and their impact on procedural efficiency, detection of gaps, procedural and cumulative radiofrequency time, and long-term outcomes. (2) Introduction of applicable criteria for gap assessment with automatic tagging and presentation of a model for evaluating lesion effectiveness using objective biophysical characteristics correlating with long-term clinical success. (3) Confirmation of significant improvement in quality of life after pulmonary vein isolation for atrial fibrillation.

Critical remarks

My critical remarks concern the following points: (1) The literature review still contains some unnecessary sections weakly related to the dissertation topic. (2) The possible combinations of values of the parameters studied for automatic tagging are extremely numerous; however, only one such combination has been investigated, and it remains unclear whether a better one exists. Yet, I have to point out that the investigation of all possible combinations is impractical and impossible. (3) Baseline differences in EQ-VAS and EQ index between groups disappear at follow-up (Table 3); therefore, an intra-group longitudinal comparison ("before" vs. "after") would be appropriate to exclude disproportionate contribution from one group. (4) Analysis of the ablation lesion characteristics (Tables 5 and 6) reveals significant differences between the two groups with regard to minimum and maximum pulmonary vein impedance (accounting for the observed differences in percentage impedance drop), application duration, mean power (with direct implications for delivered energy and impedance reduction), and the number of passes. While such differences are not unexpected in a non-randomized study, I believe that some of them can be attributed primarily to baseline differences in the ablation protocol at the center using manual tagging compared with the other two centers. (5) The pooled mean duration of follow-up appears to correspond to the maximum follow-up duration in the two centers using automatic annotation; consequently, the reported mean value reflects longer follow-up at the center using manual annotation (Fig. 11). This may limit the validity of comparisons of clinical success beyond month 40. Nevertheless, the author appropriately acknowledged the absence of a significant difference in recurrence-free survival. (6) References 6 and 276 are the same bilingual publication.

The aforementioned critical remarks do not pertain to the main positive findings of the present dissertation and, as such, do not diminish either the reported results or the scientific merit of the contributions presented in this work.

The 75-page abstract accurately and concisely presents the study aims, methods, main results, conclusions, and contributions and meets the requirements of ACC Tokuda.

Dr. Krasimir Dzhinsov has published three papers related to the dissertation: one abstract and one full-text paper in an international journal indexed in Embase and EBSCO, and one full-text paper in a Bulgarian medical journal indexed in Scopus, all as first author. After taking into account the number of co-authors, I calculated the total score to be 40, which exceeds the minimum national requirements. The two full-text papers have one citation each in Scopus-indexed journals. Six congress participations without published abstracts are also listed.

Based on the above, I conclude that the aims and objectives of the dissertation have been fulfilled and that the work meets the requirements for an independent, original scientific study addressing a major problem in medicine.

I evaluate the dissertation positively and recommend that the esteemed members of the scientific jury and the Academic Council of Acibadem City Clinic Tokuda – Sofia vote in favor of awarding the educational and scientific degree "Doctor" to Dr. Krasimir Rosenov Dzhinsov.

Sofia, 18 January 2026

Prepared by:

/Prof. T. Shalganov, MD, PhD/