M U N I

COMMENTARY TO HABILITATION THESIS[1]

Non-invasive and Invasive Approaches in Contemporary Cardiac Electrophysiology

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Brief characteristic of the investigated matter

Contemporary cardiac electrophysiology encompasses a broad range of non-invasive and invasive methods used both to advance our understanding of the physiology and pathophysiology of cardiac rhythm and to guide the management of heart rhythm disorders. Although the standard electrocardiogram (ECG) is universally available, advanced ECG-derived markers can be translated into clinical practice only when their physiological determinants, heart-rate dependence, measurement precision, and reproducibility are clearly defined. Similarly, the clinical benefit of invasive electrophysiology depends not only on continued technological advances but, above all, on a thorough understanding of cardiac anatomy, the arrhythmogenic substrate, and the pathophysiology of specific arrhythmias, together with a comprehensive and individualised approach to the diagnosis and treatment of each patient.

The habilitation thesis integrates two complementary lines of research. The first focuses on the digital analysis of atrial and atrioventricular conduction, the spatial characteristics of ventricular depolarisation, and the dynamic properties of ventricular repolarisation. The second addresses the contemporary clinical management of common arrhythmias, particularly atrial fibrillation, with a primary focus on catheter ablation procedures.

The unifying theme is the translation of accurate measurement of cardiac electrical activity into clinically meaningful interpretation and treatment. The included publications therefore range from physiological and methodological studies in healthy volunteers to prospective clinical registries, first-in-human interventional research, national guideline documents, and focused clinical reviews.

Objectives of the work

The objectives of the non-invasive part were to establish physiological reference characteristics and methodological standards for advanced ECG analysis. The studies evaluated the heart-rate dependency and sex differences of the PQ interval [1], biological determinants and spatial organisation of ventricular depolarisation [2-4], and dynamic properties of ventricular repolarisation [5-10]. Particular aims included improving the precision of QT measurement, assessing the validity of generic heart-rate correction formulae,

[1] The commentary must correspond to standard expectations in the field and must include a brief characteristic of the investigated matter, objectives of the work, employed methodologies, obtained results and, in case of co-authored works, a passage characterising the applicant's contribution in terms of both quality and content.

identifying determinants of short-term QT variability, evaluating pharmacological effects on repolarisation dynamics, and defining physiological properties of J-T subintervals.
The objectives of the invasive and clinical part were to improve the characterisation and treatment of clinically important arrhythmias. These studies assessed pulmonary vein anatomy before atrial fibrillation ablation [11], evaluated a novel low-voltage multipulse method for termination of atrial fibrillation [12] and investigated procedural and long-term determinants of outcome after catheter ablation of long-standing persistent atrial fibrillation [15-17]. Further objectives were to evaluate the feasibility and safety of near-zero or zero-fluoroscopy ablation of supraventricular arrhythmias in routine practice [18].
Some of the publications were included in the habilitation thesis to demonstrate the recognition of the applicant's expertise within the scientific and professional community. His inclusion among the authors of the Czech Society of Cardiology's national guidelines for the diagnosis and treatment of both atrial fibrillation [13-14] and ventricular arrhythmias [19] reflects his professional competence and clinical experience in the field of arrhythmology. The final publication reflects the applicant´s specific clinical and academic interest in the field of arrhythmias in adults with congenital heart disease [20].

Employed methodologies

The electrocardiographic studies used large datasets of digital 12-lead ECGs derived predominantly from Holter recordings obtained in healthy volunteers. Hundreds of thousands of 10-second ECG samples were analysed using computer-assisted signal processing followed by expert visual verification. The methods employed included morphology matching, repeated beat and segment comparisons, subject-specific regression modelling, correction for heart-rate hysteresis, analysis of beat-to-beat variability, vectorial and spatial analyses of QRS and T-wave characteristics, and comparisons according to sex, ethnic origin, and heart rate [1–8,10]. One pharmacological study used a randomised, double-blind, three-period crossover design to compare two doses of atorvastatin with placebo [9].

The atrial fibrillation studies combined imaging, invasive electrophysiology, and prospective follow-up. Pulmonary vein morphology was evaluated using computed tomography angiography and three-dimensional reconstruction in 771 patients [11]. The first-in-human study of multipulse therapy enrolled 42 patients at six centres and involved the iterative optimisation of low-voltage pulse sequences during atrial fibrillation ablation procedures [12].

The studies of long-standing persistent atrial fibrillation were based on prospective clinical registries of consecutive patients undergoing stepwise radiofrequency catheter ablation. The methodology included detailed procedural documentation, repeated rhythm monitoring, assessment of sinus rhythm restoration and arrhythmia inducibility, echocardiographic evaluation, measurement of NT-proBNP concentrations, cardiopulmonary exercise testing, quality-of-life assessment, and long-term follow-up [15–17].

The AALARA registry was a prospective, observational, multicentre, multinational study evaluating the routine use of three-dimensional mapping to reduce radiation exposure during the ablation of supraventricular arrhythmias [18]. The guideline and review publications were based on a structured evaluation of the available evidence, expert interpretation, and the translation of research findings into clinically applicable recommendations [13,14,19,20].

Obtained results

The studies of cardiac conduction demonstrated a markedly non-linear relationship between the PQ interval and heart rate, with this relationship being particularly pronounced in women [1]. QRS duration differed according to sex and ethnic origin and showed substantial interindividual variability [2]. Further work provided a detailed physiological description of the spatial distribution of the 12-lead QRS complex [3] and demonstrated systematic sex differences among different expressions of the spatial QRS–T angle, although none showed a consistent universal relationship with heart rate [4].

The repolarisation studies demonstrated that individual ECG descriptors reflect different physiological components and exhibit distinct dynamic responses [5]. Systematic morphology matching significantly improved the precision of QT interval measurement [6]. Generic QT correction formulae introduced substantial heart-rate-dependent instability, with the Bazett formula performing particularly poorly [7]. Short-term QT variability was influenced more strongly by recording and measurement quality than by beat-to-beat RR variability [8]. Atorvastatin did not induce clinically relevant adverse changes in dynamic repolarisation parameters in healthy subjects [9]. Sex, ethnic origin, and heart rate were shown to influence the J–Tend, J–Tpeak, and Tpeak–Tend intervals [10].

Among patients undergoing atrial fibrillation ablation, atypical pulmonary vein anatomy was common, with a common left ostium representing the most frequent anatomical variant [11]. In the first-in-human study, low-voltage multipulse therapy terminated 37 of 52 treated atrial fibrillation episodes during the efficacy phase, corresponding to a success rate of 71%, at energy levels substantially lower than those used for conventional electrical cardioversion [12]. The national guideline documents provided a comprehensive framework for the diagnosis and management of atrial fibrillation [13,14].

The prospective ablation studies demonstrated that the successful restoration and maintenance of sinus rhythm in patients with long-standing persistent atrial fibrillation were associated with measurable functional benefits. A composite assessment demonstrated improvements in exercise capacity, ventricular function, biomarker levels, and quality of life [15]. Restoration of sinus rhythm during the initial procedure and non-inducibility of arrhythmia at the final repeat procedure were major predictors of long-term arrhythmia-free survival [16]. A separate prospective study documented improvements in left atrial appendage flow velocity, left ventricular ejection fraction, maximal oxygen consumption, NT-proBNP concentrations, and quality of life following successful ablation [17].

The AALARA registry demonstrated that the routine use of three-dimensional mapping enabled zero-fluoroscopy procedures in almost 90% of patients and was associated with high acute success rates, low complication rates, and low recurrence rates at six months [18]. The Czech translation and adaptation of the guidelines on ventricular arrhythmias and the prevention of sudden cardiac death supported the implementation of contemporary evidence-based risk stratification and treatment strategies in Czech clinical practice [19]. The review of arrhythmias in adults with congenital heart disease summarised the complex interplay among congenital anatomy, surgical scars, haemodynamic loading, catheter ablation, device therapy, and the prevention of sudden cardiac death, while emphasising the importance of management in specialised centres [20].

Applicant's contribution

The habilitation thesis contains 20 publications. The applicant was first author of four publications [1,8,9,20] and corresponding author of one additional publication [11]. In the ECG studies, he participated in study conception, expert electrocardiographic measurements, validation of signal morphology, data analysis and interpretation, and manuscript preparation. He led the grant project and the principal clinical and scientific work underlying the atorvastatin study [9]. In the invasive studies, the applicant contributed to patient selection, catheter ablation procedures, clinical follow-up, interpretation of imaging and electrophysiological findings, data analysis, and preparation of manuscripts. As corresponding author of the pulmonary vein morphology study [11], he coordinated the clinical interpretation and publication process. In the multicentre studies, he represented an actively recruiting and interventional centre and contributed clinical data and expert interpretation [12,18]. In the guideline and review publications, the applicant contributed to the conception of the documents, critical review of the literature, formulation of clinically applicable recommendations, and drafting and revision of the text [13,14,19,20]. The documented overall contribution to individual publications ranged from 10% to 90%. The category-specific percentages below translate the qualitative contribution statements recorded in the habilitation thesis into the four categories required by the faculty template; they should be interpreted as the applicant's share within each activity rather than as values intended to sum across a row.

Bibliographic records of published scientific results included in the habilitation thesis

Accessibility and Web of Science (WoS) classifications

[1] Toman O, Hnatkova K, Smetana P, Huster KM, Sisakova M, Barthel P, Novotny T, Schmidt G, Malik M. Physiologic heart rate dependency of the PQ interval and its sex differences. Scientific Reports. 2020;10:2551.

Accessible at doi: 10.1038/s41598-020-59480-8.

Publication type and classification: Original publication. WoS classification: Multidisciplinary Sciences Q1.

Applicant's documented contribution: 30%. Study conception, electrocardiographic measurements, interpretation of statistical results, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
35	10	60	35

[2] Hnatkova K, Smetana P, **Toman O**, Schmidt G, Malik M. Sex and race differences in QRS duration. Europace. 2016;18:1842-1849.

Accessible at doi: 10.1093/europace/euw065.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q1.

Applicant's documented contribution: 20%. Study conception, electrocardiographic measurements, data analysis, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	5	25	20

[3] Hnatkova K, Andrsova I, **Toman O**, Smetana P, Huster KM, Sisakova M, Barthel P, Novotny T, Schmidt G, Malik M. Spatial distribution of physiologic 12-lead QRS complex. Scientific Reports. 2021;11:4289.

Accessible at doi: 10.1038/s41598-021-83378-8.

Publication type and classification: Original publication. WoS classification: Multidisciplinary Sciences Q2.

Applicant's documented contribution: 20%. Study conception, electrocardiographic measurements, data analysis, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	5	25	20

[4] Andrsova I, Hnatkova K, **Toman O**, Sisakova M, Smetana P, Huster KM, Barthel P, Novotny T, Schmidt G, Malik M. Intra-subject stability of different expressions of spatial QRS-T angle and their relationship to heart rate. Frontiers in Physiology. 2022;13:939633.

Accessible at doi: 10.3389/fphys.2022.939633.

Publication type and classification: Original publication. WoS classification: Physiology Q2.

Applicant's documented contribution: 20%. Study conception, electrocardiographic measurements, data analysis, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	5	25	20

[5] Hnatkova K, **Toman O**, Sisakova M, Novotny T, Malik M. Dynamic properties of selected repolarization descriptors. Journal of Electrocardiology. 2010;43:588-594.

Accessible at doi: 10.1016/j.jelectrocard.2010.06.003.

Publication type and classification: Original publication. WoS classification: Proceedings Paper.

Applicant's documented contribution: 20%. Study conception, electrocardiographic measurements, data analysis, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	5	25	20

[6] Hnatkova K, Smetana P, **Toman O**, Bauer A, Schmidt G, Malik M. Systematic comparisons of electrocardiographic morphology increase the precision of QT interval measurement. Pacing and Clinical Electrophysiology. 2009;32:119-130.

Accessible at doi: 10.1111/j.1540-8159.2009.02185.x.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q3.

Applicant's documented contribution: 20%. Study conception, electrocardiographic measurements, data analysis, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	5	25	20

[7] Andrsova I, Hnatkova K, Sisakova M, **Toman O**, Smetana P, Huster KM, Barthel P, Novotny T, Schmidt G, Malik M. Influence of heart rate correction formulas on QTc interval stability. Scientific Reports. 2021;11:14269.

Accessible at doi: 10.1038/s41598-021-93774-9.

Publication type and classification: Original publication. WoS classification: Multidisciplinary Sciences Q2.

Applicant's documented contribution: 10%. Electrocardiographic measurements, data analysis, interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
15	0	15	5

[8] Toman O, Hnatkova K, Sisakova M, Smetana P, Huster KM, Barthel P, Novotny T, Andrsova I, Schmidt G, Malik M. Short-Term Beat-to-Beat QT Variability Appears Influenced More Strongly by Recording Quality Than by Beat-to-Beat RR Variability. Frontiers in Physiology. 2022;13:863873.

Accessible at doi: 10.3389/fphys.2022.863873.

Publication type and classification: Original publication. WoS classification: Physiology Q2.

Applicant's documented contribution: 30%. Study conception, electrocardiographic measurements, data analysis, interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
35	10	60	45

[9] Toman O, Novotny T, Sisakova M, Hnatkova K, Andrsova I, Parenica J, Poloczek M, Jenysova R, Manouskova L, Spinar J, Malik M. Effect of atorvastatin on dynamic parameters of myocardial repolarization in healthy subjects. Journal of Electrocardiology. 2012;45:752-757.

Accessible at doi: 10.1016/j.jelectrocard.2012.06.020.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q3.

Applicant's documented contribution: 70%. Study conception, leadership of the related grant project, electrocardiographic measurements, data analysis, interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	5	25	20

[10] Hnatkova K, **Toman O**, Sisakova M, Smetana P, Huster KM, Barthel P, Novotny T, Schmidt G, Malik M. Sex and race differences in J-Tend, J-Tpeak, and Tpeak-Tend intervals. Scientific Reports. 2019;9:19880.

Accessible at doi: 10.1038/s41598-019-56328-8.

Publication type and classification: Original publication. WoS classification: Multidisciplinary Sciences Q1.

Applicant's documented contribution: 30%. Study conception, electrocardiographic measurements, data analysis, interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	5	25	20

[11] Farkasova B, **Toman O**, Pospisil D, Mikova M, Hejtmankova N, Zouharova A, Krikavova L, Fiala M, Sepsi M, Kala P, Novotny T. Pulmonary Vein Morphology in Patients Undergoing Catheter Ablation of Atrial Fibrillation. Cardiovascular Engineering and Technology. 2024;15:616-622.

Accessible at doi: 10.1007/s13239-024-00738-x.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q3.

Applicant's documented contribution: 20%. Study conception, assessment of imaging findings, catheter ablation procedures, data analysis, clinical interpretation, corresponding-author coordination, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
20	45	50	45

[12] Ng FS, **Toman O**, Petru J, Peichl P, Winkle RA, Reddy VY, Neuzil P, Mead RH, Qureshi NA, Whinnett ZI, Bourn DW, Shelton MB, Kautzner J, Sharma AD, Hocini M, Haissaguerre M, Peters NS, Efimov IR. Novel Low-Voltage MultiPulse Therapy to Terminate Atrial Fibrillation. JACC: Clinical Electrophysiology. 2021;7:988-999.

Accessible at doi: 10.1016/j.jacep.2020.12.014.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q2.

Applicant's documented contribution: 20%. Study conception, catheter ablation procedures, patient follow-up, data analysis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
25	5	25	15

[13] Čihák R, Heinc P, Haman L, Fiala M, Neužil P, **Toman O**. Fibrilace síní. Cor et Vasa. 2011;53(Suppl 1):27-52.

Accessibility: No DOI assigned; available through the journal archive.

Publication type and classification: National guideline publication. Indexed in Scopus; no WoS classification.

Applicant's documented contribution: 15%. Document conception, critical review of the literature, formulation of recommendations, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	10	20	15

[14] Čihák R, Heinc P, Haman L, Fiala M, Neužil P, **Toman O**. Diagnostic and treatment guidelines developed by the Working Group for Arrhythmias and Permanent Cardiac Pacing of the Czech Society of Cardiology [Fibrilace síní: doporučený diagnostický a léčebný postup České kardiologické

společnosti vypracovaný Pracovní skupinou arytmie a trvalé kardiostimulace]. Vnitřní lékařství. 2012;58(Suppl 1):1S41-1S69.

Accessibility: No DOI assigned; available through the journal archive.

Publication type and classification: National guideline publication; no WoS classification.

Applicant's documented contribution: 15%. Document conception, critical review of the literature, formulation of recommendations, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	10	20	15

[15] Fiala M, Bulkova V, Sknouril L, Nevralova R, **Toman O**, Januska J, Spinar J, Wichterle D. Functional improvement after successful catheter ablation for long-standing persistent atrial fibrillation. Europace. 2017;19:1781-1789.

Accessible at doi: 10.1093/europace/euw282.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q1.

Applicant's documented contribution: 10%. Study conception, patient selection, catheter ablation procedures, follow-up, data analysis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
15	0	10	10

[16] Fiala M, Bulkova V, Sknouril L, Nevralova R, **Toman O**, Januska J, Spinar J, Wichterle D. Sinus rhythm restoration and arrhythmia noninducibility are major predictors of arrhythmia-free outcome after ablation for long-standing persistent atrial fibrillation: a prospective study. Heart Rhythm. 2015;12:687-698.

Accessible at doi: 10.1016/j.hrthm.2015.01.004.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q1.

Applicant's documented contribution: 10%. Study conception, patient selection, catheter ablation procedures, follow-up, data analysis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
15	0	10	10

[17] Fiala M, Wichterle D, Bulkova V, Sknouril L, Nevralova R, **Toman O**, Dorda M, Januska J, Spinar J. A prospective evaluation of haemodynamics, functional status, and quality of life after

radiofrequency catheter ablation of long-standing persistent atrial fibrillation. Europace. 2014;16:15-25.

Accessible at doi: 10.1093/europace/eut161.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q2.

Applicant's documented contribution: 10%. Study conception, patient selection, catheter ablation procedures, follow-up, data analysis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
15	0	10	10

[18] Amin M, Abdrakhmanov A, Kropotkin E, Traykov V, Sallo Z, Geller L, Lorgat F, Sapelnikov O, **Toman O**, Al-Muti K, Aljaabari M, Bystriansky A, Kornyei L, Mujovic N, Simons S, Szegedi N. Ablation of Supraventricular Arrhythmias With as Low as Reasonably Achievable X-Ray exposure (AALARA): Results of Prospective, Observational, Multicenter, Multinational, Open-Label Registry Study on Real World Data Using Routine Ensite 3D Mapping During SVT Ablation. Pacing Clin Electrophysiol. 2024;47:1441-1448.

Accessible at doi: 10.1111/pace.15075.

Publication type and classification: Original publication. WoS classification: Cardiac and Cardiovascular Systems Q3.

Applicant's documented contribution: 10%. Patient selection, catheter ablation procedures, follow-up, data acquisition, data analysis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
15	0	10	5

[19] Peichl P, Bulava A, **Toman O**, Kautzner J. 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: translation of the shortened document prepared by the Czech Society of Cardiology. Cor et Vasa. 2023;65:186-235.

Accessible at doi: 10.33678/cor.2023.023.

Publication type and classification: Guideline translation and review publication WoS classification: Cardiac and Cardiovascular Systems Q4.

Applicant's documented contribution: 25%. Document conception, critical review of the literature and guideline evidence, translation, synthesis, clinical interpretation, and manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	10	30	25

[20] Toman O, Zatočil T, Koc L, Žáková D, Fiala M. Arrhythmias in patients with adult congenital heart disease. Interv Akut Kardiol. 2023;22:173-179.

Accessible at doi: 10.36290/kar.2023.029.

Publication type and classification: Review publication; no WoS classification

Applicant's documented contribution: 90%. Overall conception, comprehensive review and synthesis of the literature and guidelines, clinical interpretation, and principal manuscript preparation.

Experimental work (%)	Supervision (%)	Manuscript (%)	Research direction (%)
0	50	90	90