Institution: Imperial College London

Unit of Assessment: 01 Clinical Medicine

Title of case study: Improved accuracy of cardiac ablation by widespread implementation of Ripple Mapping

Period when the underpinning research was undertaken: 2006-2019

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Prapa Kanagaratnam	Professor of Cardiology Honorary Professor	1998 - 2001, 2001 - present
Nicholas Linton	Clinical Senior Lecturer	2006 - 2012, 2014 - present
Darrel Francis	Professor of Cardiology	2006 - present
Nicholas Peters	Professor of Cardiac Electrophysiology	1995 - present
Michael Koa-Wing	Clinical Research Fellow, then Honorary Clinical Senior Lecturer	2005 - 2008, 2008 - present
Shahnaz Jamil-Copley	Clinical Research Fellow	2010-2013
Vishal Luther	Clinical Research Fellow	2014 – 2017, Honorary to present
George Katritsis	Honorary Clinical Research Fellow	2018 - present

Period when the claimed impact occurred: 2014 - present

Is this case study continued from a case study submitted in 2014? No

1. Summary of the impact (indicative maximum 100 words)

Successful ablation of cardiac arrhythmias requires accurate localization of the origin of the aberrant myocardial electrical activity. Ripple Mapping was developed at Imperial College to provide visual 3D representation of tachycardias during patient electrophysiological studies, facilitating anatomical interpretation of the arrhythmia. It increases the success rate and reduces the time needed for curative thermo-ablation compared to conventional manual mapping. The patent is licensed to Biosense-Webster and the technology accessed via a drop-down menu in Johnson & Johnson's commercial CARTO® CONFIDENSE® Module. Ripple Mapping is recognised in the current European Society of Cardiology Guidelines and used in over 3,000 hospitals worldwide.

2. Underpinning research (indicative maximum 500 words)

The successful treatment of cardiac tachy-arrhythmias by thermo-ablation requires accurate localisation of the origin of the aberrant electrical activity. This can be done manually but it makes it a lengthy procedure for the patient, even with a highly trained member of staff. It is also subject to error as it is dependent on arbitrary choices; specifically, determining when a new electrical pulse begins so as to localize the source. This is very difficult to achieve in a

standardized manner when pulses have a wide variety of different shapes arising on a dynamic electrical background.

Human eyes are very good at detecting even subtle fluctuations in a wide expanse of visual data. Prof Kanagaratnam and colleagues at Imperial College used computer modelling to devise a novel method, Ripple Mapping, that affords 3D visualisation of the intracardiac electrogram during electrophysiological studies of the patient.

The concept was first described using data from six individuals; three with atrial tachycardias, two with ventricular tachycardias and one person in sinus rhythm (1). It used novel software to construct a three-dimensional surface from imported electrograms and demonstrate voltage and timing information for all six individuals. It demonstrated how electrical activation of the myocardium could be tracked visually and assist identification of the mechanism of tachycardias and localize the optimal ablation site without the need for an experienced computer-operating assistant. This was possible due to core expertise in applying mathematical solutions in cardiac problems.

On the basis of this report, Biosense Webster licensed the technology and integrated it into a prototype research version of their widely used clinical heart mapping system, “CARTO”. This was then evaluated and improved through a series of studies led by the Imperial team. The first refined the algorithm to streamline the method for data collection and map interpretation algorithm to optimize Ripple Maps in atrial tachycardias (2). The second showed utility in visualising the regions of subtle, slow conduction occurring adjacent to the scar of a myocardial infarction in the left ventricle (3). The relevance of this critical step is that it is these particular points at which ventricular tachycardia can be exquisitely sensitive to a curative ablation in the cath lab. The third study in this series showed that Ripple Mapping is effective in identifying the key pathways in atrial tachycardia (4). Encouraged by these data, Johnson & Johnson progressed Ripple Mapping from a tool in development and incorporated it as a permanent feature in their commercial anatomical electro-mapping system, CARTO®, now installed in thousands of hospitals across the world.

A landmark Ripple-AT multi-centre study (5) led by Imperial College with Barts, Papworth, Nottingham, Bournemouth and Lisbon randomised 105 patients with atrial tachycardia to Ripple Mapping or conventional mapping and found that Ripple Mapping enabled a substantially higher success rate (90% versus 71%) in curing the tachycardia with one set of ablations. A further publication from the trial revealed potential future advances that could make it even easier for operators using Ripple Mapping for the first time to interpret the maps quickly and accurately (6).

3. References to the research (indicative maximum of six references)

(1) Linton, N.W., Koa-Wing, M., Francis, D.P., Kojodjojo, P., Lim, P.B., Salukhe, T.V., Whinnett, Z., Davies, D.W., Peters, N.S., O'Neill, M.D., Kanagaratnam, P. (2009). Cardiac ripple mapping: a novel three-dimensional visualization method for use with electroanatomic mapping of cardiac arrhythmias. *Heart Rhythm*; 6(12):1754-62. DOI.

(2) Koa-Wing, M., Nakagawa, H., Luther, V., Jamil-Copley, S., Linton, N., Sandler, B., Qureshi, N., Peters, N.S., Davies, D.W., Francis, D.P., Jackman, W., Kanagaratnam, P. (2015). A diagnostic algorithm to optimize data collection and interpretation of Ripple Maps in atrial tachycardias. *Int J Cardiol*; 199: 391-400. DOI.

(3) Jamil-Copley, S., Vergara, P., Carbucicchio, C., Linton, N., Koa-Wing, M., Luther, V., Francis, D.P., Peters, N.S., Davies, D.W., Tondo, C., Della Bella, P., Kanagaratnam, P. (2015). Application of ripple mapping to visualize slow conduction channels within the infarct-related left ventricular scar. *Circ Arrhythm Electrophysiol*; 8(1): 76-86. DOI.

(4) Jamil-Copley, S., Linton, N., Koa-Wing, M., Kojodjojo, P., Lim, P.B., Malcolme-Lawes, L., Whinnett, Z., Wright, I., Davies, W., Peters, N., Francis, D.P., Kanagaratnam, P. (2013). Application of ripple mapping with an electroanatomic mapping system for diagnosis of atrial tachycardias. *J Cardiovasc Electrophysiol*; 24(12): 1361-9. DOI.

(5) Luther, V., Cortez-Dias, N., Carpinteiro, L., de Sousa, J., Balasubramaniam, R., Agarwal, S., Farwell, D., Sopher, M., Babu, G., Till, R., Jones, N., Tan, S., Chow, A., Lowe, M., Lane, J., Pappachan, N., Linton, N., Kanagaratnam, P. (2017). Ripple mapping: Initial multicenter experience of an intuitive approach to overcoming the limitations of 3D activation mapping. J Cardiovasc Electrophysiol; 28(11):1285-1294. DOI.

(6) Luther, V., Agarwal, S., Chow, A., Koa-Wing, M., Cortez-Dias, N., Carpinteiro, L., de Sousa, J., Balasubramaniam, R., Farwell, D., Jamil-Copley, S., Srinivasan, N., Abbas, H., Mason, J., Jones, N., Katritsis, G., Lim, P.B., Peters, N.S., Qureshi, N., Whinnett, Z., Linton, N.W.F., Kanagaratnam, P. (2019). Ripple-AT Study: A Multicenter and Randomized Study Comparing 3D Mapping Techniques During Atrial Tachycardia Ablations. *Circ Arrhythm Electrophysiol*; 12: e007394. DOI.

Grants Awarded;
British Heart Foundation CRTF (£153,492) FS/15/12/31239 Jan 2015
Biosense Webster Ripple-AT Study (£80,000) (July 2016)
Biosense Webster Ripple-VT Study (£143,000) (April 2019)

4. Details of the impact (indicative maximum 750 words)

Ripple Mapping is a novel technique that permits 3D visual representation of cardiac tachycardias during patient electrophysiological studies. It facilitates the accurate localization of the origin of the arrhythmia and guides curative thermo-ablation without the need for an experienced computer-operator assistant.

The Patent (reference US8838216B2) for this novel technique was filed by Prof Kanagaratnam with Imperial Innovations in May 2008 and granted in the United States in September 2014 [**A**]. The presentation of the initial concept (1) led to an intellectual property license agreement between Imperial Innovations and Biosense-Webster, a Johnson & Johnson company, in 2013. The agreement obtained exclusive rights to Ripple Mapping to commercialise the technique and distribute a licensed product. It also covered future costs and patent maintenance. Johnson & Johnson then incorporated Ripple Mapping as a permanent feature of their commercial CARTO® CONFIDENSE® Module with seamless access using a drop-down tab procedure [**B**]. This was introduced to the market in 2015 and it has now been rolled-out to 3,000 hospitals worldwide.

Johnson & Johnson offer a Ripple Mapping Training program at their Education Centre in Hamburg and ad hoc courses have also run in the UK, US, China, Singapore. The company also features 'The Value of Ripple Mapping' as one of their on-demand learning modules for healthcare professionals [**C**], describing the technique as 'resulting in a greater understanding in complex arrhythmia diagnosis'. There are several on-demand learning videos available through the training platform [**D**].

The studies conducted by the Imperial team (5) are referenced in the 2019 European Society of Cardiology Guidelines for the Management of Supraventricular tachycardia [**E**]. It has been adopted and exhibited by cardiac electrophysiology laboratories outside of Imperial College, using patient case studies to demonstrate the advantages of the technique for optimising identification of suitable sites for ablation. These case studies, available on YouTube, have been viewed several thousand times [**F, G**]. Ripple Mapping is the only technology that has been tested in a randomised controlled study of acute outcomes (6). Competing technologies such as Precision® (Abbot Medical) and Rhythmia® (Boston Scientific) have not been tested in any prospective, randomised controlled studies.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[**A**] https://patents.google.com/patent/US8838216B2/en Archived here.

[**B**] CARTO® CONFIDENSE™ Module with Ripple Mapping | J&J Medical Devices (jnjmedicaldevices.com). Archived here.

[**C**] The Value of Ripple Mapping: https://www.youtube.com/watch?v=jLzL0yKZkBg (archived here).
https://jnjinstitute.com/en-us/online-profed-resources/resources/value-ripple-mapping

[**D**] On-demand training videos from the Johnson & Johnson education platform: https://jnjinstitute.com/en-emea/global-search?search_api_fulltext=ripple+mapping (Archived here)

[**E**] International Guidelines:
2019 ESC Guidelines for the management of patients with supraventricular tachycardiaThe Task Force for the management of patients with supraventricular tachycardia of the European Society of Cardiology (ESC). Brugada J, Katritsis DG, Arbelo E, Arribas F, Bax JJ, Blomström-Lundqvist C, Calkins H, Corrado D, Deftereos SG, Diller GP, Gomez-Doblas JJ, Gorenek B, Grace A, Ho SY, Kaski JC, Kuck KH, Lambiase PD, Sacher F, Sarquella-Brugada G, Suwalski P, Zaza A; ESC Scientific Document Group. *Eur Heart J*. 2019 Aug 31 https://doi.org/10.1093/eurheartj/ehz467 . (References 584, 585 and 588).

[**F**] Case Study: Ripple Mapping Dr. Brenyo - YouTube (Archived here)

[**G**] Case Study: Ripple Mapping Dr. Atwater - YouTube (Archived here)