NICE advice

KODEX-EPD for cardiac imaging during ablation of arrhythmias

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is the KODEX-EPD system. It is used for cardiac imaging and navigation during ablation of cardiac arrhythmias.
- The **innovative aspects** are that the KODEX-EPD system offers real-time, high-definition imaging that visualises 3D cardiac anatomy during electrophysiology procedures and allows for an indication of ablation quality once the ablation has been done. It can also reduce radiation exposure during procedures that need fluoroscopy, such as cryoablation.
- The intended **place in therapy** would be as an alternative to existing 3D mapping systems in people with cardiac arrhythmias who are having treatment with an ablative technology.
- The **main points from the evidence** summarised in this briefing are from 6 studies (4 observational studies, 1 case series and 1 single-arm study) including a total of 132 people. They show that the KODEX-EPD system can create 3D real-time and high-resolution images without additional imaging such as fluoroscopy.

- **Key uncertainties** around the evidence or technology are that half of the studies were reported in conference abstracts only, and only 1 small case series was done in the UK.
- The **cost** of the KODEX-EPD system is £300,000 per unit, and about £1,000 to £3,000 for consumables, depending on case type (cryo- or radiofrequency ablation, excluding VAT). The company states that the maintenance contract is in line with other 3D mapping systems, priced at about £12,000 per year. Standard care is existing 3D mapping systems and costs about £700 to £3,000 for consumables.

The technology

The KODEX-EPD system (Philips Medical Systems Nederland BV) is a non-fluoroscopic 3D cardiac imaging and navigation (mapping) system. It is an open-platform catheter-based cardiac electrophysiology system that works with any validated electrophysiology catheter and uses a novel dielectric energy source. This allows electrophysiologists to electrically image unique characteristics of the heart and detail the heart wall and other structures. The sensor can be contact or non-contact on the heart wall, giving a before and after view, and provides detailed images of structures. Dielectric imaging creates real-time, high-definition 3D images of a patient's cardiac structures, without using ionising radiation or contrast media or touching the endocardium. The system can guide physicians during ablation treatment of cardiac arrhythmias and reduces the need for X-ray imaging. The company states that the system can provide this imaging in as little as 3 minutes.

The system consists of 2 units:

- a KODEX-EPD processing unit that connects multiple components including 7 dielectric sensors, a diagnostic catheter pin box, a recording pin box and a foot pedal
- a KODEX-EPD workstation.

The KODEX-EPD system also needs a key that unlocks software modules specific to whether the treatment is cryo- (freezing) or radiofrequency- (heating) based.

Innovations

The KODEX-EPD system could give real-time information of heart muscle characteristics and an indication of ablation quality once the lesion has been applied. The company claims

that using KODEX imaging would reduce exposure of radiation to both patients and healthcare professionals during ablation procedures. This claim is specifically for cryoballoon procedures because assessment of pulmonary vein occlusion can be done without the need for fluoro- or contrast injection. The company also claims that KODEX-EPD visualises patient-specific anatomical details to allow personalised therapy planning and delivery.

Current care pathway

Cardiac arrhythmias can be treated with catheter ablation if medication has not been effective or tolerated. During the ablation procedure, continuous X-ray (fluoroscopy) and a 3D mapping system (such as KODEX-EPD) are used to visualise the catheters and find the source of abnormal electrical activity, respectively. Continuous X-ray (fluoroscopy) may not be needed for all techniques but must be used with cryoballoon ablation. In the procedure, catheters are guided through the veins into the heart, where electrical activity is recorded. Once the source of abnormal electrical activity is found, an energy source is spread through the catheter to destroy the diseased area and interrupt the abnormal electrical circuits. The most common methods are radiofrequency ablation using heat, or cryoablation using freezing. Laser energy and ultrasound energy are less commonly used in the NHS. The procedure usually takes 2 to 3 hours and may be done under sedation or general anaesthesia.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on atrial fibrillation: diagnosis and management
- NICE's interventional procedures guidance on percutaneous endoscopic laser balloon pulmonary vein isolation for atrial fibrillation
- NICE's interventional procedures guidance on percutaneous balloon cryoablation for pulmonary vein isolation in atrial fibrillation
- NICE's interventional procedures guidance on percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation
- NICE's medtech innovation briefing on AcQMap for mapping the heart atria to target ablation treatment for arrhythmias.

Population, setting and intended user

The KODEX-EPD system is indicated for catheter-based atrial and ventricular mapping in people for whom electrophysiology studies are indicated. This includes people with atrial fibrillation, atrial flutter, supraventricular tachycardias and ventricular tachycardias.

KODEX-EPD is exclusively used by cardiac electrophysiology specialists who are fluent in cardiac catheterisation and ablation procedures. The technology is used in standard electrophysiology procedure environments (catheter labs).

The company states that instructions for use are provided as part of the device labelling and that training is needed and provided during system handover. The training is included in the costs of the device.

Costs

Technology costs

The KODEX-EPD visualisation and mapping system costs £300,000 with a price reduction for NHS use. The company states that the maintenance contract is in line with other 3D mapping systems, priced at about £12,000 per year. The KODEX-EPD system lifespan is 7 years.

The company states that the cost for treatment with KODEX-EPD depends on the type of arrhythmia and the consumables selected. Cost for treatment with KODEX-EPD could range from about £1,000 in a cryo- procedure to about £2,000 for less complex procedure disposable packs for radiofrequency, up to about £3,000 for complete atrial fibrillation disposable packs. These packs include a key, sensors and catheters.

For cryoablation, the catheters are not provided by the company and need to be sourced from other vendors. KODEX-EPD disposables for cryo- procedures are the cryo- sensor and key kit, which costs £1,000.

For radiofrequency ablation, the company provides the following packs:

- The radiofrequency atrial fibrillation kit costs £2,600. It includes a contact-force-enabled ablation catheter, a 20-pole pulmonary vein catheter, a coronary sinus decapolar catheter and a radiofrequency sensor and key.
- The radiofrequency flutter kit costs £2,100. It includes a contact-force-enabled ablation catheter, a coronary sinus decapolar catheter and a radiofrequency sensor and key.

Costs of standard care

- Standard-irrigated radiofrequency ablation catheter: £700.
- Complete-irrigation radiofrequency ablation catheters for atrial fibrillation (including pulmonary vein and coronary sinus catheters combined): £1,550. This excludes 3D mapping.
- Specialist contact-force-enabled catheter to be used with other mapping systems: £1,250.
- Cryoablation catheter: about £2,000.
- 3D mapping atrial fibrillation procedure with contact-force-enabled catheter: over £2,500.

Resource consequences

The company states that the KODEX-EPD system is currently used in 3 NHS trusts and that they are engaging with other trusts.

It states that the technology costs more than current standard care but has greater benefits. The company claims that KODEX-EPD maintains the speed of cryoballoon ablation but reduces exposure to radiation for both patient and healthcare professional. With cryoballoon ablation, a second procedure with a radiofrequency catheter may be necessary. Both procedures can be done with the KODEX-EPD system, saving the need for, and cost of, additional imaging technologies.

The company claims that KODEX-EPD is designed for integration into catheter labs and can be mobile for use in multiple labs, with no changes needed to the existing infrastructure.

Regulatory information

The KODEX-EPD system is a CE-marked class IIa medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Older people (aged over 65), men and people with chronic conditions such as high blood pressure are more likely to have cardiac arrhythmias. Age, gender and disability are protected characteristics under the Equality Act (2010).

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six studies are summarised in this briefing, including a total of 132 people.

The included studies are 4 comparative observational studies, 1 case series and 1 single-arm study. There are further studies that are not summarised here.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The evidence is of low-to-moderate methodological quality, and all studies are small in terms of patient numbers. Three studies were reported in conference abstracts only. Only

1 study was done in the UK. The evidence suggests that KODEX-EPD can create 3D real-time and high-resolution images to enable catheter navigation, without the need for additional imaging such as fluoroscopy. Further evidence comparing the KODEX-EPD system with standard care is needed, with a large sample size.

Maurer et al. (2019)

Study size, design and location

Observational study of 20 people with symptomatic atrial fibrillation or left atrial tachycardia scheduled for an ablation procedure in Germany.

Intervention and comparator

The KODEX-EPD system and the CARTO 3 system.

Key outcomes

Using the KODEX-EPD system, the left atrial imaging was completed within a median of 9.7 (7.5 to 12.8) minutes. The median procedure time was 97.5 (90 to 112.5) minutes, and median total fluoroscopy time was 8.2 (5.7 to 10.6) minutes, of which a median of 1.4 (1.1 to 2.3) minutes was used to create the left atrial map. Both the KODEX-EPD system and CARTO 3 measurements correlated well with fluoroscopy measurements, as reflected by Pearson's correlation coefficients (r) of 0.91 and 0.95, respectively. Bland-Altman plots revealed that, on average, KODEX-EPD measurements underestimated fluoroscopy measurements by 0.04 mm (95% limits of agreement of -5.72 mm and 5.64 mm). CARTO 3 measurements underestimated fluoroscopy measurements by 0.02 mm (95% limits of agreement of -3.61 mm and 3.57 mm). There were no procedural complications.

Strengths and limitations

The novel wide-band dielectric KODEX mapping system has the potential to create 3D real-time and high-resolution images of left atrial anatomy in CT-like quality without the need for additional imaging. This study is an early experience of high-resolution cardiac imaging using KODEX-EPD, so there is no data available for a standalone approach for left atrial mapping. The study sample size was small and may be underpowered to detect quantitative differences in the navigational accuracy between the different imaging modes. One author has received research grants and is a consultant to EPD Solutions and

Philips.

Romanov et al. (2019)

Study size, design and location

Prospective, single-centre, non-randomised, non-blinded, open-label, single-arm study of 22 people with paroxysmal atrial fibrillation refractory to antiarrhythmic drug treatments in Russia.

Intervention and comparator

The KODEX-EPD system.

Key outcomes

KODEX-EPD showed all major anatomical landmarks relevant to intracardiac catheter placement and navigation. The right atrium showed the inferior vena cava and right atrium junction, superior vena cava and right atrium junction, coronary sinus, fossa ovalis, Thebesian valve, and tricuspid valve. The left atrium showed each transseptal site, all pulmonary vein ostia, left atrium appendage orifice and mitral valve. A right accessory top pulmonary vein, a rare but clinically important anatomical pulmonary vein drainage variation, was also clearly identified. A CT image confirmed the presence of this variation.

Strengths and limitations

This study suggests that KODEX-EPD can accurately enable catheter navigation and enable real-time mapping of atrial anatomy with a high level of anatomical detail. The authors suggested that next steps include validating the system's ability to integrate cardiac electrical activity within the high-definition image.

Abeln et al. (2020)

Study size, design and location

Observational study of 26 people having cardiac ablation in the Netherlands.

Intervention and comparator

The KODEX-EPD system.

Key outcomes

Ablations were done for atrial fibrillation in 13 people (50.0%): atrial flutter in 10 (38.5%), atrial tachycardia in 1 (3.8%), atrioventricular-nodal re-entrant tachycardia in 1 (3.8%), atrioventricular re-entrant tachycardia in 2 (7.7%) and ventricular extrasystole in 2 (7.7%). The median procedure time was 99.5 (68.8 to 112.3) minutes, and median fluoroscopy time was 14.4 (10.0 to 16.9) minutes. All procedures were successful. There were no adverse events during follow up.

Strengths and limitations

This study suggests that KODEX-EPD is a novel system for cardiac mapping and anatomical imaging and can be used safely and effectively for a variety of cardiac arrhythmia ablations. The study is reported in conference-abstract form only and so is limited in detail.

Taylor et al. (2020)

Study size, design and location

Pilot case study of 6 people having cryoballoon ablation in the UK.

Intervention and comparator

The KODEX-EPD system compared with contrast venograms.

Key outcomes

There were 58 pulmonary vein occlusions verified with both contrast venography and the KODEX-EPD system. Of the 52 pulmonary veins indicated as occluded on the KODEX-EPD system pulmonary-vein-occlusion tool, 37 were satisfactorily occluded on contrast venography. Of the 6 pulmonary veins displayed as not occluded on the pulmonary-vein-occlusion tool, 3 were satisfactorily occluded on contrast venography. The sensitivity and specificity of the KODEX-EPD system occlusion tool for pulmonary vein

occlusion, as defined by contrast venography, were 92.5% and 16.7%, respectively. The positive and negative predictive values of the occlusion tool were 71.2% and 50%, respectively. There were 4 pulmonary veins that had grade 4 occlusion on contrast venography, and all were identified as occluded with the occlusion tool.

Strengths and limitations

This study suggests that the KODEX-EPD system could substantially reduce fluoroscopy exposure. However, the current software version may not currently have sufficient diagnostic accuracy to replace contrast venography. This study is reported in conference-abstract form only and so is limited in detail.

Cauti et al. (2021)

Study size, design and location

Prospective observational study in 28 people with paroxysmal or persistent atrial fibrillation having cryoballoon ablation in Italy.

Intervention and comparator

The KODEX-EPD system compared with angiogram.

Key outcomes

A total of 105 pulmonary vein cryoballoon occlusions were tested. The new occlusion tool software module showed 91% sensitivity and 76% specificity in assessing a complete pulmonary vein occlusion, verified with contrast medium injection. The positive predictive value was 80%, and the negative predictive value was 88.6%. Mean procedure time was 81, plus or minus 17 minutes. Mean fluoroscopy time was 6, plus or minus 2 minutes. No 30-day complications were observed.

Strengths and limitations

The authors state that this is the first study to assess the safety, feasibility, and efficacy of the use of a new tool. This study suggests that KODEX-EPD was able to assess the degree of pulmonary vein occlusion during a cryoballoon ablation with good sensitivity and

specificity.

Schillaci et al. (2020)

Study size, design and location

Observational study of 40 people with atrial fibrillation having cryoballoon catheter ablation in Italy.

Intervention and comparator

The KODEX-EPD system compared with no KODEX-EPD system (fluoroscopy).

Key outcomes

There were 20 patients who had the procedure under fluoroscopy guidance before the new system introduction, while 20 patients had the procedure under fluoroscopy and KODEX-EPD guidance with its occlusion tool software. The total time of the procedure was comparable between the 2 groups (90.15 minutes, plus or minus 28.67 compared with 80.77 minutes plus or minus 17.17 using the dielectric imaging system, p=0.34). Fluoroscopy time was significantly lower in the group using KODEX-EPD (16.92 minutes plus or minus 8.96 compared with 5.54 minutes plus or minus 2.06, p<0.01). Acute isolation was achieved in all pulmonary veins. No 30-day complications were observed.

Strengths and limitations

The authors state that this is the first study to show the feasibility of a reduced fluoroscopy workflow using KODEX-EPD. This study is reported in conference-abstract form only and so is limited in detail.

Sustainability

The company provided no details about sustainability.

Recent and ongoing studies

- Prospective Procedural Data Collection for Continuous Improvement of the KODEX - EPD System Performance (KODEX). ClinicalTrials.gov Identifier: NCT04552665. Status: recruiting. Indication: cardiac arrhythmia. Device: The KODEX-EPD system. Expected completion date: October 2021. Country: US.
- Evaluating the Performance of the KODEX-EPD CRyOballoon Occlusion Feature in Patients with Atrium Fibrillation (PROOF). ClinicalTrials.gov Identifier: NCT04293198. Status: recruiting. Indication: atrium, fibrillation; ablation. Device: The KODEX-EPD system. Expected completion date: April 2021. Countries: Belgium and US.
- All Inclusive KODEX - EPD Study Patient Specific Optimized Therapy (PSOT) Study (PSOT). ClinicalTrials.gov Identifier: NCT03481413. Status: not yet recruiting. Indication: arrhythmia. Device: The KODEX-EPD system. Expected completion date: December 2021. Country: not specified.
- Dielectric Tissue Imaging in Cavotricuspid Isthmus Ablation (ERUCA). Clinical Trial.gov. Identifier NCT04438395. Status: recruiting. Indication: atrial fibrillation and flutter. Device: The KODEX-EPD system. Expected completion date: September 2020. Country: US.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All 4 experts were familiar with the technology but only 2 had used this technology before.

Level of innovation

All experts agreed that the KODEX-EPD system is a minor variation compared with existing systems but has novel aspects. Innovative aspects include dielectric tissue imaging and characterisation. Experts said it also has the potential to enhance the safety of the procedure, shorten procedure times, allow for non-contact 3D anatomical maps, and provide data on lesion quality and tissue thickness. Three experts were aware of competing technologies in the NHS including the CARTO, Rhythmia, Precision and NavX

system. Most of these systems use contact mapping and can only use specific catheters.

Potential patient impact

The main patient benefit mentioned by the experts is reduced radiation exposure from ablation procedures. Two experts identified 2 groups of people who would particularly benefit from KODEX-EPD. These are people who are allergic to contrast when cryoballoon ablation is needed and people who need pulmonary-vein isolation procedures for atrial fibrillation. One expert said that it could benefit when used as first line treatment for atrial fibrillation ablation and other 'simple' ablation procedures. If this were the case, another expert said that it could be used in several thousand cases per year.

Potential system impact

The experts noted several system impacts including that a wider choice of catheters, potentially faster procedures and improved radiofrequency ablation may lead to reduced risk of damage to extra-cardiac structures. One expert said that it can enhance access because the technology can be used in catheter labs not fully equipped for electrophysiology procedures, to deliver simple ablation procedures. All experts agreed that no changes were needed to clinical facilities.

Three experts noted that currently the KODEX-EPD system is used in addition to current standard care and is therefore likely to cost more. Two experts said that the technology costs more. One expert said that if it is used as an alternative to current standard care it is likely to cost the same or even less. Two experts noted that the staff costs, procedure duration and setting are likely to be the same.

Two experts agreed that specific training is needed on how to use the technology. Two experts said that it is relatively easy to use, with 1 expert stating that it should only be used by cardiologists with electrophysiology expertise and an electrophysiology-trained catheter laboratory team. None of the experts were aware of any safety concerns around this technology. However, 2 experts said that the technology is still in development and has not yet been tested in large-scale clinical trials.

General comments

All experts agreed that the KODEX-EPD system could replace standard care. However, the

experts also agreed that the technology needs further clinical development and advances first. One expert said that this technology probably does have the potential to change or replace the current pathway, stating that it may only improve atrial fibrillation ablation outcomes marginally.

Three experts said that the cost could prevent this technology from being adopted in their organisation or across the NHS. One expert raised that the system is likely to undergo further improvement and refinement because it is currently still under development.

All experts agreed that further research is needed. One expert said that the data is limited, with small patient numbers. Another expert said that superior efficacy over existing technologies remains to be shown. Research should include randomised controlled trials to address efficacy for both cryo- and radiofrequency ablation compared with standard care.

Expert commentators

The following clinicians contributed to this briefing:

- Prof Faizel Osman, consultant cardiologist and electrophysiologist, honorary professor of cardiology (Warwick Medical School), department of cardiology, University Hospitals Coventry and Warwickshire NHS Trust. Did not declare any interests.
- Dr Moloy Das, consultant cardiologist and electrophysiologist, Freeman Hospital, The Newcastle Upon Tyne Hospitals NHS Foundation Trust. Has received speaker fees, research funding and fellowship funding from Boston Scientific. Has a consultancy agreement with the company.
- Dr John P Bourke, consultant cardiologist (electrophysiologist), Freeman Hospital, The Newcastle Upon Tyne Hospitals NHS Foundation Trust and senior lecturer, Translational and Clinical Research Institute, Newcastle University. Did not declare any interests.
- Dr Anthony Li, consultant cardiologist and electrophysiologist, Cardiology Clinical Academic Group, St. George's University Hospitals NHS Foundation Trust. Did not declare any interests.

Prof Paulus Kirchhof also commented on this medtech innovation briefing.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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