New and emerging health technologies for Parkinson’s disease

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The aim of this review was to identify new and emerging health technologies (excluding pharmaceuticals) for the diagnosis, monitoring, treatment and rehabilitation of patients with Parkinson’s disease (PD). PD presents a significant and increasing burden upon the UK National Health Service. It is the second most common neurodegenerative disorder after Alzheimer’s disease, with incidence rising with increasing age.

Searching of bibliographical databases, clinical trial registries, technology databases and other online sources was combined with consultation with clinical experts to identify relevant new and emerging health technologies.

Forty-six new and emerging health technologies for PD were identified; 19 for diagnosis, 2 for monitoring, 13 for treatment, 10 for rehabilitation and 2 cell replacement therapies. Clinical experts were asked to provide advice on each technology’s degree of innovation, potential for future impact (on patient outcomes, NHS systems and resources), current use, and any potential barriers to adoption.

A number of the health technologies identified were of particular interest.

Experts say that biomarkers are a key area for future research in the accurate and early diagnosis of PD. We identified several biomarkers which can be readily accessible clinically (cerebrospinal fluid, blood and saliva). However all the biomarkers identified in this review are still at an early stage of clinical research and issues relating to specificity and sensitivity were highlighted by experts. A known issue in diagnosing PD is the difficulty in differentiating it from other related disorders. We identified neuroimaging techniques which use radiolabelled tracers to help distinguish between Parkinsonian disorders, but experts say that the relative lack of positron emission tomography (PET) scanners within the NHS may limit the use of these techniques. In the future, it is thought that a combination of biomarker testing and neuroimaging techniques will allow for improved early diagnosis and monitoring of disease progression. Other areas of interest are the diagnosis of PD in the prodromal stages by focusing on non-motor symptoms of PD which can appear decades before motor symptoms appear. We identified tests that can detect olfactory dysfunction, speech dysfunction and eye kinetic patterns.

In treatment, we identified several new deep brain stimulation (DBS) systems exhibiting incremental changes to existing DBS systems. The new systems aim to target more accurately specific areas of the brain to allow for greater therapeutic efficacy with fewer side effects. We also identified novel brain targets for DBS to treat symptoms such as dementia which is not possible with current DBS treatment. Not all patients with PD are suitable for DBS treatment. We identified a non-invasive alternative treatment that uses magnetic resonance (MR) ultrasound to treat essential tremor.

In rehabilitation, an expert commented on the importance of simple and cost effective aids which would not be perceived as being too complex or ‘high tech’. We identified one such aid which uses a laser device mounted to any walking roller or cane, to serve as a visual cue. Exercise programmes to help with gait disturbances and balance were also identified but experts commented that exercise has small short term effects on motor function with little impact on quality of life, and trial data on efficacy is still awaited.
Currently there is no cure for PD but research is looking at human foetal tissue to halt or slow disease progression. The TRANSEURO project started to recruit patients into its trial in mid 2013 but due to ethical and other related issues it is unlikely that human foetal tissue transplantation will be adopted into NHS clinical practice in the near future.

Experts comment that although this is time of great innovation for the diagnosis and treatment of PD, most of the health technologies identified in this review are still at an early stage of development. Further well designed trials and data on the efficacy and applicability of the technologies are required before these can be considered for adoption in clinical practice.

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1. INTRODUCTION

This review was conducted for the National Institute for Health and Care Excellence (NICE). It is intended to provide the Medical Technologies Evaluation Pathway and Diagnostic Assessment Programme at NICE with horizon scanning intelligence on new and emerging technologies for the diagnosis, monitoring, treatment and rehabilitation of patients with Parkinson’s Disease (PD).

1.1 CLINICAL NEED AND BURDEN OF DISEASE

Parkinson’s disease (also known as idiopathic PD and primary parkinsonism) is a progressive neurodegenerative disorder of the central nervous system. In PD there is a loss of dopaminergic cells in the substantia nigra, a region of the midbrain. PD predominantly leads to complications with movement, such as tremor, muscle stiffness or rigidity and bradykinesia. As the disease progresses, non-motor symptoms such as depression, apathy, pain, sleep disturbances, dysphagia, weight loss and cognitive impairment increasingly affect quality of life. These symptoms can occur at any stage of disease and many precede a formal diagnosis of PD by several years. The Hoehn and Yahr scale is a commonly used staging system to describe the progression of PD symptoms.

PD is estimated to affect 100-180 people per 100,000 of the UK population, which approximates to between 55,692 and 125,000 people in England and Wales. There is a rising prevalence with age and a higher prevalence and incidence of PD in males. Most people with PD are older than 50 years, but about 1 in 20 develop their first symptoms aged less than 40 years. Approximately 1% of the population aged over 65 years has PD, rising to 2% in those over 80 years. In 2011, 3,710 deaths due to PD were registered in England and Wales.

1.2 RELEVANT GUIDANCE

NICE Guidance

Other Guidance
- European Federation of Neurological Societies. Late (complicated) Parkinson’s disease. 2011.

1.3 CURRENT PRACTICE

DIAGNOSIS AND MONITORING

Confirming diagnosis of PD can be difficult as PD develops gradually over years and shares symptoms with other parkinsonian disorders. There is no definite diagnostic test to confirm PD and it is recommended that people with suspected PD are referred quickly, untreated, to a specialist with expertise in the differential diagnosis of PD. PD is diagnosed after a clinical examination using the Parkinson's brain bank criteria. Single Photon Emission Computed Tomography (SPECT) may be used to exclude other conditions with similar symptoms.

People diagnosed with PD should be reviewed every 6-12 months and the diagnosis reconsidered if atypical symptoms develop.

TREATMENT AND REHABILITATION

There is no cure for PD and treatment is aimed at relieving both motor and non-motor symptoms and slowing progression of disease. Treatment includes:

- Pharmacologic - Levodopa, dopamine agonists, MAO-B inhibitors.
- Surgical therapy – restricted to a small number of patients. The main approaches are:
  - Deep brain stimulation (thalamic, pallidal and subthalamic stimulation).
  - Lesioning (pallidotomy, thalamotomy and subthalamotomy).
- Gamma knife surgery.

Rehabilitation aims to maintain and improve mobility, flexibility, strength, gait speed, and quality of life. This can include physiotherapy, occupational therapy and speech and language therapy.

1.4 AIM & OBJECTIVE

The aim of this review was to identify new and emerging health technologies for use across the care pathway of patients with PD (see appendix 1).

This report, which has been informed by consultation with clinical experts, is not intended to provide a comprehensive overview of all new and emerging health technologies for PD, but to report on those most likely to have an impact on the care pathway and associated healthcare resources.
2. METHODS

2.1 INCLUSION CRITERIA

Health technologies (not including pharmaceutical technologies) for PD that were within the following time window of development or commercial availability were the main focus of the review:

- Emerging – defined as in development and expected to be CE marked within the next 18 months.
- New – defined as already licensed and have been CE marked or launched in the UK for 24 months or less.

2.2 SEARCH STRATEGY

A combination of searching online and in-house sources of intelligence and consultations with experts in the field was used to identify new and emerging health technologies across the entire care pathway (see appendix 1).

Online sources included:

- Technology databases and reports: the HTA programme and Medica.
- Members only access of the EuroScan International Network database of new and emerging health technologies.
- Bibliographical databases: Medline, Embase and the Cochrane library.
- Research in progress: Clinical trial registries e.g. ClinicalTrials.gov.
- Clinica Medtech Intelligence (http://www.clinica.co.uk/) for intelligence on medical technologies for PD.
- Conference reports and abstracts from specialist journals.
- General internet searching using Google to access medical media reports, review articles, industry press releases, etc.

In-house intelligence:

- NIHR Horizon Scanning Centre database of new and emerging technologies.

Consultation with experts:

- Six clinical experts and three medical organisations/societies were contacted and invited to suggest any relevant technologies.
- Once a list of technologies had been identified through the search process, participating experts were invited to comment on the potential significance of the technologies.

Full details on the methods used can be found in appendix 2.
3. RESULTS

We identified 46 relevant new and emerging technologies. These were grouped into 10 tables according to the technology type and their place in the care pathway. Some technologies identified were outside the timeframe outlined in the inclusion criteria (too early), but have been included in the results to provide a complete picture of developments on the horizon for PD. The status of development of each technology identified is indicated in the tables.

Figure 1: Total number of technologies identified according to type

<table>
<thead>
<tr>
<th>Table</th>
<th>Type of technology</th>
<th>Total number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diagnosis – biomarkers</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>Diagnosis – neuroimaging</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Diagnosis – other tests</td>
<td>9</td>
</tr>
<tr>
<td>4</td>
<td>Monitoring</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Treatment – new approaches</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>Treatment – DBS targeting new therapeutic sites</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Treatment – developments in DBS</td>
<td>3</td>
</tr>
<tr>
<td>8</td>
<td>Treatment – DBS aid systems</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>Rehabilitation programmes and devices</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>Cell replacement therapies</td>
<td>2</td>
</tr>
<tr>
<td>Technology name</td>
<td>Company/ developer</td>
<td>Technology description</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>----------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>NuroPro blood test for 57 protein</td>
<td>Amarantus BioScience</td>
<td>Diagnostic platform which monitors the concentration of 57 protein markers in blood serum linked to neurodegeneration. Amarantus’ license is focused on the further development of a subset of 21 of these protein markers specifically targeting early diagnosis and on-going monitoring of Parkinson’s disease.</td>
</tr>
<tr>
<td>Saliva gland biopsy for abnormal</td>
<td>Michael J. Fox Foundation for Parkinson’s</td>
<td>Biopsies of two different salivary glands: the gland under the lower jaw and the minor salivary glands in the lower lip.</td>
</tr>
<tr>
<td>Parkinson’s protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>proteins biomarkers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha-synuclein protein in colonic</td>
<td>Rush University Medical Center</td>
<td>Alpha-synuclein aggregation underlies Parkinson's disease pathology, and its presence in peripheral tissues may be a reliable disease biomarker.</td>
</tr>
</tbody>
</table>
Current usage: None
Barriers to adoption: Patient acceptability may be an issue due to invasiveness. Since early diagnosis does not yet translate into better care there may be no meaningful role for this within the NHS.

Phosphorylated alpha-synuclein protein - blood test
University of Lancaster UK
Early clinical development
http://www.medicalnewstoday.com/articles/238476.php
Innovation: High
Impact: Potentially high as a screen but yet to be proven robust in clinical practice when the diagnosis is not already clinically obvious

Current usage: None.
Barriers to adoption: Still in early development and may not be very useful unless treatment is available.

Alpha-synuclein in skin biopsies
Universidad Autonoma de San Luis Potosí
Early clinical development
http://www.neurology.org/cgi/content/meeting_abstract/78/1_MeetingAbstracts/S22.005?sid=26cd92ad-cc4d-45dc-9348-45cd8d510c38
Innovation: High
Impact: Unlikely to be high as the test is too invasive as a screen.

Current usage: Research.
Barriers to adoption: Patient acceptability may be an issue due to invasiveness. Several groups have explored this previously with inconsistent results and therefore may not have any mileage as a diagnostic test in the NHS clinical practice.

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
</table>
| 18F-AV-133 PET scans | Avid Radiopharmaceuticals | 18F-AV-133 PET scans can be used to differentiate subjects with Parkinson's Disease from other movement disorders. | Phase II/III | http://www.clinicaltrials.gov/ct2/show/NCT01550484?cond=%22Parkinson+Disease%22&phase=12&rank=1 | Innovation: Low
Impact: Potential for impact is poor as there is a low availability of PET scanners in the NHS so not likely to be used.
Current usage: None.
Barriers to adoption: Currently DaTscan is in routine clinical use within the NHS. Other imaging techniques should demonstrate equivalence or advantages before being adopted. |
<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffusion Tensor Imaging (DTI)</td>
<td>Brain Dynamics, S.L.</td>
<td>DTI is a magnetic resonance imaging modality that allows the study of the anatomical connectivity in the normal brain as well as changes in development, ageing, disease and degeneration.</td>
<td>In clinical trials</td>
<td><a href="http://www.neurology.org/cgi/content/meeting_abstract/78/1_MeetingAbstracts/S22.003?sid=9122cfc8-cd00-4ed4-9dc1-222a9e8ee81e">http://www.neurology.org/cgi/content/meeting_abstract/78/1_MeetingAbstracts/S22.003?sid=9122cfc8-cd00-4ed4-9dc1-222a9e8ee81e</a></td>
<td>Innovation: Moderate- MRI is widely available. Impact: Potential for impact on patients and NHS is poor as there is no proof of validity tests yet but the technique and infrastructure already exist to implement in the NHS context if required. Current usage: Research. Barriers to adoption: Further clinical studies are required to truly determine the value of such an approach.</td>
</tr>
<tr>
<td>Transcranial B-mode sonography</td>
<td>No company identified</td>
<td>A neuroimaging technique that displays the brain parenchyma and the intracranial ventricular system through the intact skull. Allows visualisation of characteristic changes such as substantia nigra (SN) hyperechogenicity in Parkinson’s disease.</td>
<td>In clinical trials</td>
<td><a href="http://www.biomedcentral.com/1471-2377/10/9">http://www.biomedcentral.com/1471-2377/10/9</a></td>
<td>Innovation: High – it is the first to use ultrasound for the clinical diagnosis of PD. Impact: Potential for impact is high as it is not expensive and is widely available. However approximately 15% of cases unsuitable as no bone window possible. Current usage: Research only. Barriers to adoption: Further clinical research is required before it can be used as a clinical tool. Also requires specifically trained personal to operate the equipment.</td>
</tr>
<tr>
<td>Test</td>
<td>Company</td>
<td>Description</td>
<td>Trials</td>
<td>Impact</td>
<td>Current usage: Barriers to adoption:</td>
</tr>
<tr>
<td>-------------------------------------------</td>
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</tr>
<tr>
<td>Voice analysis software (Parkinson's Voice Initiative)</td>
<td>MIT</td>
<td>A tool that uses precise voice analysis software to detect Parkinson's. It takes advantage of Parkinson's tendency to cause speech problems including reduced volume (hypophonia), reduced pitch range (monotone), and difficulty with articulation of sounds or syllables (dysarthria). Can be administered remotely.</td>
<td><a href="http://medgadget.com/2012/08/interview-with-max-little-phd-director-of-the-parkinsons-voice-initiative.html">http://medgadget.com/2012/08/interview-with-max-little-phd-director-of-the-parkinsons-voice-initiative.html</a> <a href="http://eprints.aston.ac.uk/18329/fulltext=sapir&amp;searchid=1&amp;FIRSTINDEX=0&amp;sortspec=date&amp;resourcetype=HWCIT">http://eprints.aston.ac.uk/18329/fulltext=sapir&amp;searchid=1&amp;FIRSTINDEX=0&amp;sortspec=date&amp;resourcetype=HWCIT</a></td>
<td>Innovation: High Impact: Impact could be high as it is a non-invasive proposal to diagnose PD. Current usage: None. Barriers to adoption: Usefulness in early PD may be limited when there is minimal, if any speech impairment. But if sufficiently sensitive and operator independent then could be interesting, particularly if remote analysis is possible. Still in clinical trials and further work is required before it can be used as a clinical tool.</td>
<td></td>
</tr>
<tr>
<td>Sniff Magnitude Test</td>
<td>WR Medical Electronics Co.</td>
<td>The test measures a patient's sense of smell, which can be one of the first indications of a brain disorder. Using a nasal tube attached to a plastic container, chemical vapours are released that expose a patient to different smells. The size and intensity of a subject's sniff are measured.</td>
<td><a href="http://www.mddionline.com/blog/devicetalk/sniff-test-could-indicate-brain-disorders">http://www.mddionline.com/blog/devicetalk/sniff-test-could-indicate-brain-disorders</a></td>
<td>Innovation: Low Impact: May be very useful in confirming diagnosis of PD. A test that could easily become available within the NHS. Current usage: None Barriers to adoption: Unlikely to be sufficiently sensitive or specific to enhance clinical diagnosis and may have to be combined with other screening tests.</td>
<td></td>
</tr>
<tr>
<td>Electrovestibulography (EvestG)</td>
<td>Neural Diagnostics</td>
<td>A non-invasive technique to record neural activity from the vestibular apparatus and vestibular nuclei.</td>
<td><a href="http://www.neuraldiagnostics.com/">http://www.neuraldiagnostics.com/</a></td>
<td>Innovation: Low Impact: No theoretical base to support its potential for PD diagnosis and therefore unlikely to have an impact on patient outcomes. Current usage: None. Barriers to adoption: Still in clinical trials so it's usefulness as a clinical tool is unknown.</td>
<td></td>
</tr>
<tr>
<td><strong>Fluorescent probes to detect amyloids</strong></td>
<td><strong>University of California</strong></td>
<td><strong>Proteins called amyloids mark several different, though related degenerative brain diseases including Parkinson's. Fluorescent probes are being developed that change colour depending on what type of amyloid they encounter. Because amyloids accumulate in the eye as well as the brain, it is hoped that diagnoses can be made with simple eye drops or ointment and an eye exam.</strong></td>
<td><strong>In clinical trials</strong></td>
<td><strong><a href="http://ucsdnews.ucsd.edu/pressrelease/colorcodedmarkersmayhelpdoctorsdianosepneuraldiseasesthessthroughtheeye">http://ucsdnews.ucsd.edu/pressrelease/colorcodedmarkersmayhelpdoctorsdianosepneuraldiseasesthessthroughtheeye</a></strong></td>
<td><strong>Innovation: High – not currently available. Impact: Amyloid is only useful for the detection of dementia associated with PD, and not the primary cause of the motor disease. Current usage: None Barriers to adoption: Amyloid is not directly important in PD.</strong></td>
</tr>
<tr>
<td><strong>Electromagnetic (EM) tracking sensors and a digitising tablet computer</strong></td>
<td><strong>Company not identified</strong></td>
<td><strong>Provide an objective measurement of bradykinesia. Patients produce drawings on a digitising tablet and perform finger-tapping tasks whilst wearing tracking sensors on the index finger and thumb. The data recorded is compared to clinician rated scores.</strong></td>
<td><strong>In clinical trials</strong></td>
<td><strong><a href="http://www.mdsabstracts.com/abstract.asp?MeetingID=787&amp;id=99373">http://www.mdsabstracts.com/abstract.asp?MeetingID=787&amp;id=99373</a></strong></td>
<td><strong>Innovation: Low Impact: May be useful for the assessment of bradykinesia. May play a role in disease monitoring rather than diagnosis. Could also be very important in clinical trials testing effectiveness of drugs. Current usage: Research only Barriers to adoption: Lacking diagnostic accuracy.</strong></td>
</tr>
<tr>
<td><strong>Mobile eye brain tracker</strong></td>
<td><strong>e(ye)BRAIN</strong></td>
<td><strong>Measures eye movements using high resolution cameras. The motion analysis carried out by the system aims to identify neurological conditions which manifest in subtle changes to the eye kinetic patterns.</strong></td>
<td><strong>In clinical trials</strong></td>
<td><strong><a href="http://www.medgadget.com/2011/12/keeping-an-eagle-eye-on-parkinsons-disease.html">http://www.medgadget.com/2011/12/keeping-an-eagle-eye-on-parkinsons-disease.html</a></strong></td>
<td><strong>Innovation: High Impact: Highly unlikely to be used in clinical practice. Current usage: None Barriers to adoption: Lacking diagnostic accuracy.</strong></td>
</tr>
<tr>
<td><strong>Biosensor based mobile gait analysis</strong></td>
<td><strong>Company not identified</strong></td>
<td><strong>An integrated accelerometer and gyroscope are attached to shoes allowing objective measurement of gait signals during standardized gait exercises in people with Parkinson’s disease.</strong></td>
<td><strong>CE marked 2011</strong></td>
<td><strong><a href="http://www.mdsabstracts.com/abstract.asp?MeetingID=787&amp;id=99395">http://www.mdsabstracts.com/abstract.asp?MeetingID=787&amp;id=99395</a></strong></td>
<td><strong>Innovation: Low Impact: Useful for assessment of gait in patients with PD. Could also be very important in clinical trials testing effectiveness of drugs. Current usage: None Barriers to adoption: Still in clinical trials so it's usefulness as a clinical tool is unknown. There have been many such devices over the years, none of which have been very useful.</strong></td>
</tr>
</tbody>
</table>
BioBolt
University of Michigan
An invasive brain implant that captures neural signals from within the brain and transmits them to an external device by using the skin as a conductor.
In clinical trials
Innovation: Low
Impact: No potential for high impact as the test is too invasive
Current usage: None
Barriers to adoption: a very invasive test which would only ever be used in rare surgical cases.

Table 4: Parkinson’s disease technologies - monitoring

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
</table>
Impact: Potential impact on patient therapy adjustment.
Current usage: Research only
Barriers to adoption: Many such devices over the years, none of which have been very useful. Accelerometers which are widely available are more likely to give an ecologically valid overview of activity/treatment effects. |
| Computerised tool to measure motor fatigue | No company identified. | Computerised tool to measure motor fatigue over time on a continuous scale. Subjects are asked to perform a pronation-supination type movement using a lightbulb-like device for a period of time (20-50 seconds). The bulb device records the number of turns at an adjustable sampling rate allowing for computerized analysis of the turning speed (number of turns per time unit) and rate of fatigue. | In clinical trials | http://www.mdsabstracts.com/abstract.asp?MeetingID=787&id=99385 | Innovation: Low
Impact: This device records impairment, not function or capability but may be useful in adjusting patient therapy. Current usage: Research only
Barriers to adoption: Many such devices over the years, none of which have been very useful. |
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Company/Institution</th>
<th>Description</th>
<th>Approval Date</th>
<th>Trial Information</th>
<th>Impact</th>
<th>Current Usage</th>
<th>Barriers to Adoption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extradural motor cortex stimulation (EMCS)</td>
<td>Catholic University, Rome.</td>
<td>A surgical procedure is performed to place a strip of four electrodes in an extradural location - on top of the dura.</td>
<td></td>
<td>In clinical trials</td>
<td>Innovation: High Impact: The procedure is invasive therefore potential for impact maybe low however it is likely to have less morbidity than DBS and possibly wider applicability. Current usage: None Barriers to adoption: Too invasive and development is at an early stage therefore theoretical basis for benefit is not entirely clear.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ExAblateNeuro; MR guided (cranial) focused ultrasound</td>
<td>InSightec Ltd</td>
<td>A focused ultrasound delivered through a helmet-like apparatus containing phased array focused ultrasound transducers. CT scanning is used to identify the region to direct the ultrasound to, and MRI or MR thermography can be used to track the delivery of the energy to the area. It is described as non-invasive and safe, and targeting within 1mm accuracy.</td>
<td>CE marked</td>
<td>In clinical trials</td>
<td>Innovation: High Impact: This approach may be useful in patients not suitable for DBS or not wishing to undergo DBS. Also provides an alternative non-invasive mechanism to perform ablative functioning neurosurgery. Current usage: Although CE marked, not available in the UK. Barriers to adoption: Only preliminary data is available for the management of essential tremor, which suggests that it may be useful to treat tremor secondary to PD. Not aware of any published data for its use with Parkinson's tremor.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep transcranial magnetic stimulation (TMS) system</td>
<td>Brainsway Neuronetics, Inc</td>
<td>The technology delivers targeted magnetic pulses deep into the brain, inducing electrical signals that can activate neurons in the localised region.</td>
<td>CE marked</td>
<td>In clinical trials</td>
<td>Innovation: Moderate Impact: Evidence for significant efficacy of TMS in PD is lacking and therefore unlikely to have any impact on patient care. This should be considered a research tool. Current usage: Research only. Barriers to adoption: Technology too big and impractical. Unlikely to be developed into smaller practical device.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phagenyx; neurostimulation based therapy for dysphagia</td>
<td>Phagenesis</td>
<td>Electrical impulses stimulate the nerves in the pharyngeal area, resulting in improved swallowing function and control.</td>
<td>CE marked</td>
<td>In clinical trials</td>
<td>Innovation: High Impact: Potential for severe drooling but limited applicability to wider population where botox is already quite effective. Current usage: None Barriers to adoption: There is no published data on the use of phagenyx for dysphagia in PD.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vibroacoustic Therapy (VAT) | University of Toronto | VAT, uses vibrations produced by low frequency sounds to "massage" deep parts of the body. | In clinical trials | [http://www.news.utoronto.ca/good-vibrations-using-sound-treat-disease](http://www.news.utoronto.ca/good-vibrations-using-sound-treat-disease) | Innovation: High  
Impact: Likely to have low efficacy therefore unlikely to have a basis to support its use in patients with PD.  
Current usage: None  
Barriers to adoption: Low efficacy.

Table 6: Treating Parkinson’s disease - DBS systems targeting new therapeutic sites

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/ availability</th>
<th>Useful links</th>
<th>Expert comments</th>
</tr>
</thead>
</table>
Impact: May have a role in managing gait disturbance and falls however some patients are likely to have cognitive issues so broad implementation is unlikely.  
Current usage: A few patients.  
Barriers to adoption: Data is preliminary and should be considered an investigational target and limited to pilot studies or research trials. If efficacy is demonstrated likely to be limited to specialist centres and rigorous case selection. There are also issues related to targeting and stimulation parameters. |
| Tandem DBS                          | Mayo Clinic      | Targeting the STN/GPi and fornix/hypothalamus and/or hippocampus to improve cognitive function and/or reducing risk for subsequent dementia | In clinical trials      | [http://www.prd-journal.com/article/S1353-8020(11)70053-0/abstract](http://www.prd-journal.com/article/S1353-8020(11)70053-0/abstract) | Innovation: High  
Impact: Tackles a major area of unmet need in PD – the dementia. Although unlikely to be disease modifying it could manage symptoms.  
Current usage: STN DBS is a standard treatment for advanced disease in young patients.  
Barriers to adoption: Data is preliminary and should be considered an investigational target and limited to pilot studies or research trials. Furthermore most patients are too old for such surgery because of higher stroke and death risk and the technique is invasive. |
Table 7: Treating Parkinson’s disease - Developments in DBS

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/ availability</th>
<th>Useful links</th>
<th>Expert comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synapse DBS system</td>
<td>3WIN, belgium</td>
<td>DBS system which consists of an implantable pulse generator, which has a proprietary computer chip embedded in it.</td>
<td>Unknown</td>
<td><a href="http://www.3win.be/products/synapse.php">http://www.3win.be/products/synapse.php</a></td>
<td>Innovation: High Impact: Possible. A promising device as it provides a non-invasive means of obtaining useful depth recordings over long periods of time. Current usage: STN DBS is a standard treatment for advanced disease young patients. Barriers to adoption: Most patients are too old for such surgery because of higher stroke and death risk. This work is technique ‘refining’.</td>
</tr>
<tr>
<td>SureStim; Steerable deep brain stimulation</td>
<td>Sapiens Steering Brain Stimulation</td>
<td>A steerable DBS system that is claimed will more accurately target areas of the brain for stimulation, reducing side effects associated with current forms of DBS. It has the same 1.3mm diameter of a conventional lead but with 40 plus tiny fully programmable electrodes compared to the usual 4 ring-shaped electrodes. Visualisation software is under development for positioning the device.</td>
<td>CE marking and EU launch of SureStim and SureSuite (the software) is expected in 2014.</td>
<td><a href="http://www.sapiensneuro.com/">http://www.sapiensneuro.com/</a></td>
<td>Innovation: High Impact: Possible Current usage: STN DBS is a standard treatment for advanced disease young patients. Barriers to adoption: Most patients are too old for such surgery because of higher stroke and death risk. This work is technique ‘refining’.</td>
</tr>
<tr>
<td>Vercise Deep Brain Stimulation (DBS) System</td>
<td>Boston Scientific Limited</td>
<td>Allows doctor to selectively control the electric current delivered through each electrode.</td>
<td>CE marked 2012</td>
<td><a href="http://bostonscientific.mediaroom.com/2012-09-28-Boston-Scientific-Launches-Vercise-Deep-Brain-Stimulation-System-in-Europe">http://bostonscientific.mediaroom.com/2012-09-28-Boston-Scientific-Launches-Vercise-Deep-Brain-Stimulation-System-in-Europe</a></td>
<td>Innovation: High Impact: Possible Current usage: STN DBS is a standard treatment for advanced disease young patients. Barriers to adoption: Most patients are too old for such surgery because of higher stroke and death risk. This work is technique ‘refining’.</td>
</tr>
<tr>
<td>Technology name</td>
<td>Company/developer</td>
<td>Technology description</td>
<td>CE status/availability</td>
<td>Useful links</td>
<td>Expert comments</td>
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</tr>
<tr>
<td>SpineAssist</td>
<td>Mazor Robotic</td>
<td>Doctors will be able to use SpineAssist to place electronic implants in the brain during deep brain stimulation procedures, which help mitigate the symptoms of Parkinson's disease, dystonia, chronic pain and depression.</td>
<td>CE marked</td>
<td><a href="http://www.medicalnewstoday.com/releases/224083.php">http://www.medicalnewstoday.com/releases/224083.php</a></td>
<td>Innovation: Low Impact: Potential for impact is low. Surgeons can already use a variety of methods to implant DBS leads with precision into the brain. Current usage: None. Barriers to adoption: A number of surgical robots are in existence/development already.</td>
</tr>
<tr>
<td>Simultaneous Bilateral Subthalamic Deep Brain Stimulation with Parallel Neurophysiologic Localization Data</td>
<td>FHC, Inc.</td>
<td>A virtual platform and a virtual representation of the patient's head is incorporated into the target planning software. The data are transmitted to the company for production of actual micro-targeting platforms which are affixed to the fiducial bone markers on the day of surgery along with a micro-targeting driving system for passing the DBS electrodes. Two micro-targeting platforms are fabricated (one for each hemisphere), so they can both be fixed to the six bone markers simultaneously.</td>
<td>In clinical trials.</td>
<td><a href="http://www.aans.org/Media/Article.aspx?ArticleId=17345">http://www.aans.org/Media/Article.aspx?ArticleId=17345</a></td>
<td>Innovation: High Impact: No clear benefit to the patient therefore unlikely to have any impact. Current usage: None. Barriers to adoption: A very expensive, patient customised method of performing surgery.</td>
</tr>
<tr>
<td>Tool to track real-time adenosine changes</td>
<td>Mayo Clinic</td>
<td>A novel way to monitor real-time chemical changes in the brains of patients undergoing deep brain stimulation (DBS). A fast scan cyclic voltammetry (FSCV) was used to quantify concentrations of adenosine released in patients during deep brain stimulation. The data was recorded using Wireless Instantaneous Neurotransmitter Concentration Sensing, a small wireless neurochemical sensor implanted in the patient's brain.</td>
<td>In clinical trials.</td>
<td><a href="http://www.medicaltradefair.com/cipp/md_medicacustom/pub/content.oid,38771/lang,2/ticket.g_u_e_s_t/local_lang,2">http://www.medicaltradefair.com/cipp/md_medicacustom/pub/content.oid,38771/lang,2/ticket.g_u_e_s_t/local_lang,2</a></td>
<td>Innovation: High Impact: No clinical benefit to the patient Current usage: None Barriers to adoption: Research tool only.</td>
</tr>
</tbody>
</table>
The sensor, combined with FSCV, scans for the neurotransmitter and translates that information onto a laptop in the operating room.

Table 9: Rehabilitation programmes and devices

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Patient indication</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>WalkMate System</td>
<td>Tokyo Institute of Technology</td>
<td>Gait in Parkinson patients</td>
<td>The system uses the timing of the walking person as a sensory input for the robot and the sound of a walking rhythm as the robot’s output. An algorithm based on travelling wave dynamics is used to control the timing difference between the gathered data and sound signals the device is sending to its wearers.</td>
<td>Unknown</td>
<td><a href="http://www.titech.ac.jp/bulletin/innovation.html">http://www.titech.ac.jp/bulletin/innovation.html</a></td>
<td>Innovation: High Impact: Very similar to cueing devices which are already used in clinical practice and therefore unlikely to have a major impact on patient care. Current usage: None Barriers to adoption: Unlikely to be of practical use in PD.</td>
</tr>
<tr>
<td>Mobilaser</td>
<td>Mobilaser</td>
<td>Gait in Parkinson patients</td>
<td>Mobilaser is a laser device which is being investigated to help patients overcome freezing of gait episodes.</td>
<td>CE marked</td>
<td><a href="http://www.mobilaser.org/">http://www.mobilaser.org/</a> <a href="http://medgadget.com/2011/10/research">http://medgadget.com/2011/10/research</a></td>
<td>Innovation: Moderate Impact: A simple device, highly effective in overcoming gait freezing. The advantages of fewer falls and cheap cost would suggest that it is a cost effective aid. Current usage: None – although variants of this</td>
</tr>
<tr>
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<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Wii-style video games</td>
<td>The University of California San Francisco School of Nursing and Red Hill Studios, an educational games startup</td>
<td>Gait and balance in Parkinson patients</td>
<td>Playing computer-based physical therapy exercises can help people with Parkinson's improve their gait and balance.</td>
<td>In clinical trials</td>
<td><a href="http://medgadget.com/2011/10/wii-style-video-games-showing-benefit-as-physical-therapy-for-parkinsons-disease.html">http://medgadget.com/2011/10/wii-style-video-games-showing-benefit-as-physical-therapy-for-parkinsons-disease.html</a></td>
<td><a href="http://www.clinicaltrials.gov/ct2/show/NCT01580787?term=wii">http://www.clinicaltrials.gov/ct2/show/NCT01580787?term=wii</a> rank=29</td>
</tr>
</tbody>
</table>

The Mobilaser is essentially a laser pen which can be mounted to any walking roller or cane and projects a laser generated line on the ground in front of the patient, which serves as a visual cue. [chered-demonstrate-visual-cuing-for-freezing-of-gait-using-lasers.html](http://chered-demonstrate-visual-cuing-for-freezing-of-gait-using-lasers.html)
<table>
<thead>
<tr>
<th>Device/Technology</th>
<th>Institution/Source</th>
<th>Description</th>
<th>Clinical Trials/Links</th>
<th>Barriers/Impact</th>
<th>Adoption Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-box kinect</td>
<td>Neurology Center for Neurological Care and Research</td>
<td>Gait and balance in Parkinson patients</td>
<td>Playing computer-based physical therapy exercises can help people with Parkinson’s improve their gait and balance</td>
<td><a href="http://www.neurology.org/cgi/content/meeting_abstract?ref=78/1_MeetingAbstracts/P01.176?sid=72ade357-e0ec-444f-8dcf-80d6e1a3fd28">http://www.neurology.org/cgi/content/meeting_abstract?ref=78/1_MeetingAbstracts/P01.176?sid=72ade357-e0ec-444f-8dcf-80d6e1a3fd28</a></td>
<td>Innovation: Low Impact: Possibility of tailoring exercise to individual needs and a therapy acceptable to most patients. Current usage: Some patients. Barriers to adoption: Patients need to demonstrate a significant “carry-over” effect from the time of performing the exercises. Cost and availability could also be barriers to implementation.</td>
</tr>
<tr>
<td>Epidural stimulation</td>
<td>University of California, Los Angeles, Medtronic</td>
<td>Motor function in patients with Parkinson patients</td>
<td>Stimulator was used to provide continual direct “epidural electrical stimulation” of the lower spinal cord to mimic the signals that the brain normally sends to initiate movement.</td>
<td><a href="http://medgadget.com/2011/05/spinal-neurostimulation-helps-paraplegic-man-stand-step-and-move-legs.html">http://medgadget.com/2011/05/spinal-neurostimulation-helps-paraplegic-man-stand-step-and-move-legs.html</a></td>
<td>Innovation: High Impact: Low – major issues with invasiveness and patient acceptability. Current usage: None Barriers to adoption: Too invasive and costly to be useful.</td>
</tr>
<tr>
<td><strong>HandTutor system</strong></td>
<td><strong>Medi-Touch</strong></td>
<td><strong>Motor function in patients with Parkinson patients</strong></td>
<td><strong>Novel system designed to evaluate and support the rehabilitation of sensory, motor and cognitive hand impairments. System is composed of a glove worn by the patient that acts like a computer mouse, and the MediTutor support software. A disposable glove is used inside the HandTutor system to reduce the risk of cross-infection.</strong></td>
<td><strong>CE marked in February 2009.</strong></td>
<td><strong><a href="http://www.handtutor.com/">http://www.handtutor.com/</a></strong></td>
</tr>
</tbody>
</table>

| **Respiratory muscle strength training** | **University of Florida** | **Respiratory muscle strength training** | **Behavioural treatment approach—high intensity respiratory muscle strength training (MST)—for blunting of facial expressions in people with PD. The MST device, a mouthpiece that the participant uses to inspire against resistance, may improve the strength and In clinical trials.** | **http://www.clinicaltrials.gov/ct2/show/NCT00350402?cond=%22Parkinson+Disease%22&phase=12&rank=45** | **Innovation: Low**<br>**Impact: Low – not likely to act upon hypomimia. However may have multiple possible uses including anxiety and dyskinesia.**<br>**Current usage: None**<br>**Barriers to adoption: Usefulness in patients with PD still unknown.** |
mobility of muscles around the mouth that are involved in forming facial expressions.

<table>
<thead>
<tr>
<th>Technology</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibion PK100/Power knee</td>
<td>Ossur, Tibion Bionic Technologies</td>
<td>Motor function in patients with Parkinson patients</td>
<td></td>
<td>CE marked 2011</td>
<td><a href="http://www.tibion.com/">http://www.tibion.com/</a></td>
</tr>
</tbody>
</table>

Table 10: Cell replacement therapies for Parkinson disease

<table>
<thead>
<tr>
<th>Technology name</th>
<th>Company/developer</th>
<th>Technology description</th>
<th>CE status/availability</th>
<th>Useful links</th>
<th>Expert comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human foetal dopaminergic cell therapy</td>
<td>FP7 funded consortium</td>
<td>The TRANSEURO consortium is also looking at foetal tissue of the midbrain containing dopaminergic neuroblasts.</td>
<td>Preclinical trials or early clinical trials.</td>
<td><a href="http://www.transeuro.org.uk/pages/disease.html">http://www.transeuro.org.uk/pages/disease.html</a></td>
<td>Innovation: High Impact: Trials have just started, and if successful will have a high impact on patient outcomes, however it is unlikely to be widely</td>
</tr>
</tbody>
</table>
applicable/implemented in the NHS.
Current usage: Research.
Barriers to adoption: Many issues ranging from ethical to case selection to the symptoms treated. Furthermore cell therapy does not alter progression of non-dopaminergic complications like dementia.
4. Overview of findings

4.1 DIAGNOSTICS

Making an accurate diagnosis of PD, especially in the early stages of disease is difficult and is largely based on clinical criteria. This review identified two main areas of research in diagnosis; biomarkers and neuroimaging. Other investigational diagnostic modalities were also identified, which focussed on clinical markers for motor symptoms and diagnostic markers for non-motor symptoms.

Given the complex nature of PD it is unlikely that a single diagnostic test will be able to differentially diagnose PD. The future of diagnosing PD will rely upon a combination of clinical, laboratory, imaging and genetic data such as those identified in this review.

4.1.1 DIAGNOSIS – BIOMARKERS

The misdiagnosis rate of PD can range from 10-50% partly due to the fact that there are no sensitive and specific validated biomarkers to differentiate PD from other parkinsonian disorders. In this review we identified both invasive and non-invasive tests that analyse a number of biomarkers for PD from clinically readily accessible samples such as blood, saliva, cerebrospinal fluid (CSF) and skin biopsies.

Alpha-synuclein has been researched intensely as a biomarker for PD and this review identified three samples from which it could be extracted; skin biopsy, blood plasma and colonic tissue. Although experts commented on the innovativeness of these tests, issues over sub-optimal sensitivity and specificity may limit the role of alpha-synuclein in the early diagnosis of PD until further research proves its diagnostic capabilities.

Experts also highlighted the importance of non-invasive tests. Blood based screening tests for PD such as the NuroPro blood test (Amarantus Bioscience) have potential for high impact in terms of securing early and accurate diagnosis if shown to be sufficiently sensitive and specific. Whereas invasive diagnostic tests such as the saliva gland biopsy and CSF sample for abnormal PD proteins are unlikely to be appropriate for clinical practice due to patient acceptability.

Diagnosing PD using biomarkers is a key area for further research. The biomarkers identified in this review are still very early in clinical research and although they have potential are unlikely to be adopted into clinical practice in the near future. Issues over sensitivity and specificity, test re-test reproducibility, expense and invasiveness need addressing. An expert commented that if an accurate biomarker was to be discovered there is still a question regarding its usefulness in the absence of an effective disease modifying treatment for PD.

4.1.2 DIAGNOSIS – NEUROIMAGING

Neuroimaging aims to differentiate between different parkinsonian disorders. In this review we found various imaging modalities which are being actively researched and developed.

SPECT is widely available within the NHS and proven to enhance diagnostic accuracy but is unable to differentiate typical from atypical parkinsonian disorders. This review identified the use of radiolabelled tracers such as 18F-AV-133 in positron emission
tomography (PET) scans to differentiate between parkinsonian disorders. However, experts comment that the limited availability of PET scanners in the NHS makes this an unlikely technique to be adopted into wider clinical practice. Although radiolabelled tracer imaging shows promise not only as a diagnostic tool but also as a measure of disease severity and progression, the associated costs and logistics would probably make this test more suitable as a second tier confirmatory test after, first tier, less costly screening tests.

An active area of research in neuroimaging markers is assessing brain function beyond dopaminergic degeneration and this includes magnetic resonance imaging (MRI) and transcranial sonography (TCS). TCS is an established technique which holds future promise in the prodromal diagnosis of PD. TCS is widely available, inexpensive and non-invasive, however its relatively low specificity precludes its use in isolation as a diagnostic test, and its inability to achieve adequate bone windows, particularly in older adults, can interfere in testing in up to 15% of patients.

Although MRI is not a new technology and is widely available it is particularly useful in ruling out secondary causes of parkinsonism. Diffusion Tensor Imaging (Brain Dynamics, S.L.) is a recent advance in MRI which may provide an index of cell loss in the substantia nigra. This could provide a marker for early degenerative or pathological processes in PD which may be helpful in prodromal diagnosis of PD.

4.1.3 DIAGNOSIS – CLINICAL MARKERS
There are various clinical markers that can be used to diagnose both motor and non-motor symptoms in PD. A biosensor based mobile gait analysis device which allows objective measurement of gait was identified as well as an electromagnetic tracking sensor and digitising tablet computer which measures bradykinesia. Experts commented that these quantitative, computerised assessments of motor performance may be useful in a research setting where the effectiveness of drugs are tested in clinical trials, but are unlikely to gain widespread accepted use in a clinical setting due to a lack of diagnostic accuracy and specificity.

Olfactory function has been studied intensely as an early screening test of detecting pre-clinical PD. The sniff magnitude test (WR Medical Electronics Co.) which measures the size and intensity of a subjects sniff could be used to distinguish PD from other parkinsonian disorders. However experts commented that the test is unlikely to be sufficiently sensitive or specific enough to enhance clinical diagnosis and may have to be combined with other screening tests. The detection of other non-motor features of PD including eye movement can be tested using a CE marked approved device called mobile eye brain tracker (E(eye) BRAIN). The ability to detect non-motor features such as this and voice analysis hold promise as a means of diagnosing premotor PD.

4.1.4 DIAGNOSIS – GENETIC TESTING
Although several single gene mutations have been identified in both familial and sporadic PD, the variable expression of such mutations has limited the use of genetic testing to identify early PD or diagnose PD. We identified a blood-based diagnostic (PDtect) for 500 genes in microarray (Diagenic). Although this is a very innovative test with potential for high impact as a screen for patients with genetic forms of PD, the test is in clinical trials and therefore its effectiveness still needs confirmation. If a blood-
based genetic test was to become available it could have huge implications in terms of disease management.

4.2 MONITORING TESTS

We identified two monitoring devices for PD both of which experts classed as low innovation but with the potential of being useful in adjusting patient therapy. Both the KinesiaHomeView™ system (Great Lakes NeuroTechnologies) which monitors motor symptoms, and a computerised tool to measure motor fatigue, are still in early trials.

4.3 TREATMENT

We identified several incremental developments in DBS systems and a number of innovative treatment approaches that manage the symptoms of PD.

4.3.1 DBS SURGERY AND SYSTEMS

DBS surgery, either of the subthalamic nucleus (STN) or the globus pallidus pars interna (GPi) is the main surgical treatment therapy for PD when motor fluctuations and dyskinesias cannot be adequately managed with pharmacological therapy. It is widely available within the NHS and NICE issued guidance on the use of DBS in people with PD in November 2003. There have since been several incremental developments to existing DBS systems which experts described as technique ‘refining’. These include a steerable DBS system (SureStim) that is claimed to more accurately target areas of the brain for stimulation and a DBS system (Vercise DBS) that allows doctors to selectively control the electric current through the electrode. A new system called Synapse DBS (3WN, Belgium) has the added functionality of non-invasively obtaining depth recordings over long periods of time. Although these developments are incremental, the improved ability to visualise brain target structures with controlled electrical field steering, may allow for greater therapeutic efficacy with fewer of the side effects commonly associated with DBS stimulation.

A major challenge in DBS surgery is targeting new therapeutic sites within the brain for the treatment of other clinical features of PD that have so far evaded effective treatment. An innovative tandem DBS system (Mayo Clinic) which targets the STN/GTi and fornix/hypothalamus and/or hippocampus tackles a major area of unmet need in PD - cognitive function and dementia. However experts commented that tandem DBS should be considered investigational and limited to pilot studies or research trials. Another novel target for DBS - pedunculopontine nucleus (PPN), is also being studied for use in conjunction with STN DBS to help treat gait disturbances and postural instability. However, like tandem DBS data is preliminary and the use of this target should be limited to pilot studies or research trials.

4.3.2 OTHER TREATMENT APPROACHES

Not all people with PD are suitable candidates for DBS and alternative surgical and treatment therapies have been developed. Extradural motor cortex stimulation (Catholic University, Rome) is a surgical procedure where a strip of four electrodes is placed in an extradural location in patients with advanced PD who are not suitable or are unresponsive to DBS surgery. Experts commented that although this is an innovative alternative therapy to DBS with less morbidity than DBS, the procedure is invasive and
development is still at an early stage and therefore theoretical basis for benefit is still unclear.

An alternative non-invasive treatment for patients was also identified. ExAblateNeuro (Insightec Ltd) is a MRI guided focused ultrasound which enables real-time treatment monitoring. This is a highly innovative treatment which was CE marked in 2012 but is not yet available for use in the UK. Experts indicated that based on preliminary data its main use will be to treat tremor secondary to PD. Another non-invasive therapy is deep transcranial magnetic stimulation (TMS). In PD it has been studied as an intervention to improve both motor and non-motor symptoms. In general, benefits when implemented have been small and short-lived however given the potential clinical benefit and limitations of medical therapy there is a need for further studies to develop and define the efficacy and benefits of TMS. Experts felt that a major barrier to the adoption of this technology was the size of the equipment.

4.4 REHABILITATION PROGRAMMES AND DEVICES

As PD progresses, patients lose postural stability, have gait dysfunction and frequent daily falls. Exercise is an integral part of the rehabilitation management of PD, and tailored exercise programmes such as Tai Chi and Wii-style video games may help to reduce balance impairments and gait function. There are several on-going trials looking at efficacy of these exercise programmes. A number of rehabilitation devices are also in development and an expert highlighted the importance of relatively simple devices which would not be perceived as being too complex or 'high tech'. One such device is the mobilaser (Mobilaser) which is essentially a laser pen that can be mounted on any working roller or cane to serve as a visual cue to the patient. Experts commented that this is an extremely simple device, and a very cost effective aid which could help reduce the number of falls.

4.5 CELL REPLACEMENT THERAPIES

None of the currently available treatment therapies can slow or halt disease progression; therefore there is a need for new therapies such as cell replacement therapy to provide both dopamine replacement but also to protect the dopamine neurons from further degeneration. Human foetal tissue has been proven in proof-of-principle evidence to provide significant function benefit in patients with PD and new trials such as the TRANSEURO project have started recruiting patients. However, human foetal tissue transplantation is unlikely to become a routine part of clinical practice due to ethical issue, and it has to be realised that cell therapies are not a cure for PD as they are unable to treat non-motor features such as dementia. An expert commented if stem cell technology is proven available and safe in the future it is more likely to supersede foetal cells transplants.

5. SUMMARY

This review identified a total of 46 health technologies, and advice was sought from clinical experts as to their degree of innovation, potential for future impact (on patient outcomes, NHS systems and resources), current use, and any potential barriers to adoption. The technologies that are likely to have the most impact in the future on diagnosis of PD are non-invasive tests such as blood-based tests for biomarkers (the NuroPro Blood test and the alpha-synuclein blood test); a neuroimaging technique
using ultrasound (transcranial B mode sonography); and voice analysis software. Earlier diagnosis may enable better disease management and an innovative blood-based genetic test (PDtect, Diagenic) which can detect genetic forms of PD is currently in clinical trials.

Current treatment options for PD aim to relieve symptoms and slow disease progression, and consist of pharmacological options and/or surgery. There have been several incremental developments to existing DBS systems but a new tandem DBS system (Mayo clinic) which simultaneously targets different areas of the brain aims to treat symptoms such as dementia and cognition function, which is not currently possible. Furthermore, for patients not suitable for DBS treatment a novel non-invasive MRI guided ultrasound treatment, ExAblateNeuro may provide an alternative treatment option. Rehabilitation is an integral part of the management of motor symptoms of PD. A simple, effective laser cue called mobilaser (Mobilaser) was highlighted by experts and could potentially reduce the number of falls experienced by people with PD. A cure or disease modifying treatment for PD does not currently exist. Research is on-going in the area of human foetal dopaminergic cell therapy (TRANSEURO project) to halt or slow disease progression but this is not a technology that will be adopted into routine clinical practice in the near future.

Experts comment that although this is time of great innovation for the diagnosis and treatment of PD, most of the health technologies identified in this review are still at an early stage of development. Further well designed trials and data on the efficacy and applicability of the technologies are required before these can be considered for adoption in clinical practice.
Early disease' refers to PD in people who have developed functional disability and require symptomatic therapy. 'Later disease' refers to PD in people on levodopa who have developed motor complication.

Palliative care requirements of people with PD should be considered throughout all phases of the disease.

1 Early disease’ refers to PD in people who have developed functional disability and require symptomatic therapy. ‘Later disease’ refers to PD in people on levodopa who have developed motor complication.
The review was carried out between October 2012 and April 2013. The steps followed in the review were:

**STEP 1: REVIEW PROTOCOL**

A review protocol was developed and agreed with the customer; the Diagnostic Assessment Pathway and Medical Technologies Evaluation Programme at NICE.

Inclusion criteria for technologies:

(a) **Technology types**
- Screening
- Prevention
- Diagnosis
- Staging
- Prediction
- Prognosis
- Treatment
- Monitoring.

(b) **Timeframe**
- Emerging – technologies in development and expected to be CE marked within the next 18 months.
- New – technologies already licensed and have been CE marked or launched in the UK for 24 months or less.

In addition to CE marked products, overseas testing services and non-commercial (e.g. ‘homebrew’) tests were included. In the time available to complete the review, it was not possible to verify the exact stage of development or adoption of all the technologies identified. The technology tables therefore include some technologies which may fall outside the requested timeframe, but are presented as they may still be of interest to policy-makers. Pharmaceutical technologies were not included.

**STEP 2: EXPERT RECRUITMENT & INITIAL CONSULTATION**

Six clinicians and three relevant professional medical organisations with expertise that spanned the clinical care pathway for Parkinson’s disease were identified and invited to provide input unto the review. Of those contacted, two clinicians and all 3 professional organisations responded. At this stage, they were asked to provide information of any relevant technologies known to them.

**STEP 3: SEARCH PROCESS**

Relevant technologies that met the inclusion criteria (or appeared likely to do so) were identified by searching the following sources:
- Our in-house HSC database of new and emerging health technologies.
- The databases and reports of other early awareness and alert agencies via the EuroScan International Network (www.euroscan.org.uk).
- Bibliographical databases, including Medline, Embase, and the Cochrane library.
- Clinical trial registries, including WHO International Clinical Trials Registry, ClinicalTrials.gov, and Current Controlled Trials.
- Conference reports and abstracts.
- Specialist journals.
- Clinica for intelligence on medical technologies for PD.
- Google to access a wide range of online sources of intelligence, including medical media reports, press releases, and review articles.

Following initial identification, information was obtained on the technologies from publicly available sources to help determine whether they should be included in the list to be put forward for the next step.

**STEP 4: IN-DEPTH CONSULTATION WITH EXPERTS**

Once the identification had been completed and inappropriate technologies and duplicates had been eliminated, the technologies were tabulated according to technology type. Basic information about each of the technologies was added to the table. Tables were then sent to the experts and professional organisations, seeking input on the following questions:

- Which technologies are innovative? What features are innovative?
- Which have potential for high impact on patient outcomes/NHS systems/resources?
- How long have they been available for, and how widely are they used currently in the NHS (and private practice)?
- Are there any barriers to adoption into NHS clinical practice?
- Have any technologies been missed that should be considered?

The purpose of this in-depth consultation with experts was to add value to the intelligence gathered, not only by clarifying the potential significance of the technologies, but also to provide a useful narrative on the state of technological development in the field and to highlight key research, evaluation and adoption issues. At this stage one professional organisation which had initially agreed to partake in this exercise did not respond with comments.

**STEP 5: FILTRATION OF TECHNOLOGIES**

Once the requested advice and intelligence had been received from the experts, this was used to filter the initial list of technologies down to a final list of technologies for inclusion in the report.
6. REFERENCES

17. Cummins G and Barker RA. What is the most promising treatment for Parkinson's disease: genes, cells, growth factors or none of the above? Regenerative Medicine 2012;7(5):617-621.

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