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7.0 Tesla magnetic resonance imaging in neurodegenerative diseases

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Methods

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Limitations

This report is based on information available when the searches were made and does not contain data on subsequent developments or improvements of the evaluated technology. The observations made on effectiveness, safety or cost-effectiveness of the technology evaluated in
the report are to be considered temporary.

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Declaration of Conflict of Interest

The authors declare that they will not receive either benefits or harms from the publication of this report. None of the authors have or have held shares, consultancies or personal relationships with any of the producers of the devices assessed in this document.

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Name of the technology/procedure: **7.0 Tesla magnetic resonance imaging in neurodegenerative diseases**

Target population

The target population which is candidate for investigation with 7.0 T high field Magnetic Resonance Imaging (7.0T MRI) includes all patients with neurodegenerative disease.

Description of the procedure and technology

7.0T MRI is proposed in order to obtain, especially in neurology, a number of advantages over lower-field (1.5T and 3.0T) [Jens M, 2009]. The greatest advantages lie in higher signal-to-noise ratio which translates into elevated spatial resolution and enables more detailed description of cerebral anatomy, pathology and molecular functionality [Mekle R, 2009]. The fMRI (functional MRI) exploration studies are of particular interest, through measurement of the BOLD (Blood Oxygen Level Dependent) signal. This effect rises with the intensity of the static magnetic field, and the perfusion and diffusion techniques where improvement of the signal-to-noise ratio enables greater precision of observation of the functional dynamics of the neural networks involved in the performance of cerebral functions [Dae-Shik K, 2003]. Other applications for the technology of reference regard:

- TOF (Time Of Flight) angiographic analyses which enable non-invasive exploration and anatomical-structural evaluation of vascular circulation [Kang CK, 2010];
- Molecular imaging which enables the visualisation in-vivo of the biochemical processes of interest;
- Spectroscopy – exploiting the magnetic properties (chemical shift), not only hydrogen, but also phosphorous 31P, carbon 13C and sodium 23Na – which lets to explore more extensively the distribution and the biological dynamics useful in the study of slow metabolisms [Wattjes MP, 2009].

Due to the elevated magnetic field, the procedure differs from lower field MRI systems and is more complex. The patient is positioned on the patient table before entering the diagnostics room. In some systems patient table moves forward on railway or on a path to reach the gantry taking into account the field lines. To avoid nervous stimulations the patient enters more carefully in the gantry. Consequently, the procedure is longer on average than those with 1.5T and 3.0T systems: the scan time may last from 20 minutes to 2 hours relative to the neuroimaging procedure [NCT00413621]. This report only assesses 7.0T MRI for diagnosis and follow-up in patients with neurodegenerative disease.

Clinical importance and burden of disease

The neurodegenerative process is defined as the progressive loss of development of basic functions or the total or partial loss of the nervous system. Alzheimer's disease, Parkinson's disease and multiple sclerosis are including the most important neurodegenerative disorders in clinical and epidemiological studies [Filiano J, 2005]. In terms of impact on the Italian population, Alzheimer's disease is the most common form of senile dementia. It currently affects some 5% of the elderly and it is estimated that there are some 500,000 persons affected in Italy [CNESPS]. This number will probably rise on the basis of demographic trends and the estimated aging of the Italian population. After Alzheimer's disease, Parkinson's disease is the most common neurodegenerative disease, affecting some 2% of the over 65 population. According to data from the ISS, there are approximately 220,000 cases of Parkinson's in Italy [CNESPS].
Multiple sclerosis (MS), or plaque sclerosis, is one of the most common diseases of the central nervous system, with chronic course, often progressively invalidating. It affects the population between 15 and 50 years of age, generally manifesting in young adults, between 20 and 30, and in females in a 2:1 ratio with respect to males. There are some 57,000 MS patients in Italy, with a total of some 1,800 new cases each year [CNESPS].
Recently, the technological evolution in Magnetic Resonance scanners allowed the development of three dimensional models of the brain which improve the observation of anatomical details, revealing even slight structural and ultra-structural modifications of the cerebral parenchyma [Tedeschi G, 2005]. Using 7.0T MRI it may be possible to recognise the specific profile of the atrophy caused by the neurodegenerative diseases which affect different cerebral regions [Tallantyre EC, 2010]. Further, the visualisation of more anatomical and functional details with respect to 1.5T and 3T MRI [Tallantyre EC, 2009], 7.0T MRI may, thus, enable early diagnosis of the neurodegenerative diseases and consequently permit, in some cases, to set a more appropriate therapeutic programme [Cho ZH, 2010], monitoring its effectiveness in the follow-up.

Products, manufacturers, distributors and approval

7.0T MRI is currently produced by the GE Healthcare, Philips S.p.A. and Siemens S.p.A. companies. None of the systems has CE marks or FDA approval and they are thus not registered in the Medical Devices Repertory of the Italian Ministry of Health. In Italy, the DPR n. 542/1994 restricts the use of static induction fields exceeding 4 Tesla to research purposes, and solely on the limbs, thus 7.0T MRI systems cannot be used in the study of the brain.

Product name	Manufacturer/Distributor	CE Mark	RDM	FDA
7T MRI 950	GE Healthcare	☐	☐	☐
Achieva 7.0T	Philips S.p.A.	☐	☐	☐
Magnetom 7T	Siemens S.p.A.	☐	☐	☐

Setting

The technology is used only in advanced research centers for clinical research and development of the technology itself.

☐ Home	☐ Hospital	☐Outpatients
☐ Accident and Emergency	☑ Other: Research centres	

Roll out in Italy

In Italy, due to the legal restrictions discussed above, 7.0T MRI systems have not been installed yet.

☑ Pre-marketing	☐ On the market for 1-6 months	☐ On the market for 7-12 months
☐ On the market for more than 12 months	☐ Not identified	

Comparators

To date 1.5T and 3.0T MRI systems are used for diagnosis and follow-up of neurodegenerative disease. These systems are considered the main comparators of 7.0T MRI.

Effectiveness and safety

The efficacy of 7.0T MRI lies in the ability to diagnose, earlier and more accurately, cerebral lesions attributable to neurodegenerative pathologies [Tallantyre EC, 2009; Kollia K, 2009]. Further, the efficacy of this technology refers to the faculty to monitor the evolution of the pathology through a more accurate follow-up of the patient [Ge Y, 2008].

A search of the literature on the use of 7.0T MRI in the diagnosis and follow-up of neurodegenerative pathology patients was conducted using the EuroScan and CRD databases (DARE & HTA) (12th November 2010), to identify Horizon scanning (HS) and rapid Health Technology Assessment reports on the specific argument, published in Italian and in English. This search produced no results.

The scientific evidence was identified considering studies published and present in the major databases: Medline (12th November 2010), Cochrane Library (12th November 2010) and Embase (12th November 2010). We included only comparative *in vivo* studies of neurodegenerative disease patients who underwent scanning with 7.0T MRI for diagnosis and follow-up of these pathologies. The comparators for the technology of reference were 1.5T and 3.0T MRI systems. The literature search identified 5 comparative studies of 7.0T MRI with respect to traditional technology at lower field (Table 1).

Four studies [Ge Y, 2008; Kollia K, 2009; Tallantyre EC, 2009; Tallantyre EC, 2010] regarded Multiple Sclerosis patients, while a single study considered only one Parkinson's patient. In total 32 Multiple Sclerosis patients and one single Parkinson's disease patient were considered.
Studies on Multiple Sclerosis patients demonstrated that 7.0T MRI, when compared with 1.5T and 3.0T technology, showed the structural anatomy of the lesions with more precision, substantially influencing the diagnostic accuracy of the method itself [Tallantyre EC, 2009]. In particular, 7.0T MRI appears to be able to highlight more accurately early changes in cerebral lesion vascularisation. This aspect is very important in the diagnosis and follow-up of the lesions [Ge Y, 2008]. It is not possible to draw any consideration regarding the effectiveness of 7.0T MRI on Parkinson's patients, since only one patient was included in the study.

The searches on the web site www.clinicaltrial.gov produced two registered clinical studies (NCT 01085253, NCT00321568) (14th December 2010): the first study, still ongoing recruitment of patients, aims to identify a new marker for the early detection of lesions caused by Parkinson's disease. The second, however, has recently ended, and was intended to use the high magnetic field generated by 7.0T MRI for the visualization of cortical lesions in different parts of the brain in patients with multiple sclerosis. The literature review conducted, however, showed no studies related to the trial completed.

The safety issues of the technology needs to be addressed with specific studies on the effects of electromagnetic fields on patients and workers. Currently in the literature there are few data regarding safety procedures with 7.0T MRI. From the first results studies show adverse effects (e. g. dizziness and nausea) increased in patients scanned with 7.0T MRI compared to 1.5T [Theysohn JM, 2008; Möller HE, 2008]. However, according to the FDA there aren't particular health risks for exposure to static magnetic fields within the 8.0T [CDRH, 1997]. As for the lower field magnetic resonance technologies, the scan cannot be performed on those with cardiac pacemakers, metallic clips, prostheses and the other categories of people for whom there are contraindications for exposure to magnetic fields (DPR No. 542 of 8.8.1994).

Potential benefits to patients

7.0T MRI could be useful in the early diagnosis of neurodegenerative diseases, enabling more accurate monitoring of patient conditions. However, to date, 7.0T MRI is still in experimental phase and there is a lack of scientific evidence supporting these considerations.

☐ Mortality reduction or increased survival	☐ Reduction of the morbidity	☐ Improved quality of life (patient/users)
☑ Improved patient monitoring	☐ Other:	☐ Not identified

Cost of the technology/procedure

The investment for the 7.0 MRI is considerable and connected with the acquisition of the technology together with the construction of suitable premises and plant. Also operating costs for specialised personnel involved and maintenance are significant. The manufacturers generally provide the technology under of agreements

and specific research projects: investments amounted to approximately € 10,000,000 in 5 years.

☐ Increased costs compared to alternative treatments	☐ Increased costs due to increased demand	☑ Increased costs due to the required investments
☐ New costs	☑ Other: Costs related to research projects	☐ Not identified

Potential structural and organisational impact

Structural impact

The structural impact of the new technology is relevant. The complexity of the technology is linked with the management and the technical problems generated by the high magnetic field which requires significant resources related with the technological investment and operating costs of the technology.
7.0T MRI must be installed in a suite designed and built specifically for the technology, able to bear the high weight of the magnet (approximately 35 tons) and of the shields (approximately 30 up to 450 tons for not shielded high homogeneity magnets). The provision of suitable path for the safety of operators and patients, as well as plant solutions for conditioning, aeration, the evacuation and expulsion of cryogen gases, oxygen detection, shut down of the magnetic field, channelling the cryogen gases and the medical gas plant are also required.

☐ Increase in requirement of instruments	☐ Always be used	☑ Can be used only under specific circumstances
☐ Decrease in requirement of instruments	☐ Other:	☐ Not identified

Organisational impact

Considering the use of 7.0T MRI exclusively in the research field, the activities involve new highly qualified professionals (as researchers in physics and engineering as well as clinics).

☐ Increase in the number of procedures	☐ Re-organisation required	☑ Training required for users
☐ Reduction in the number of procedures	☑ Other: Involve new and highly qualified professionals in technology development and management.	☐ Not identified

Conclusions

Initial analysis of the existing literature indicates that 7.0T MRI appears to be hopeful, as the elevated signal-to-noise ratio would enable the display of anatomical and functional details not visible with other, lower field systems. However, the scientific evidence is only at the beginning and the clinical impact requires further evaluation and validation. Few comparative studies, involving a small number of patients, evaluated the effectiveness of 7.0T MRI. It is expected thus more comparative and randomized trials with more cases. Moreover, there must be further investigations of the safety aspects with specific studies concerning to the effects of electromagnetic fields on patients and workers, as well as testing the positive effects for patients related to the therapeutic options available by an earlier diagnosis and more accurate follow up. The relevant costs and the need of specific professionals, able to manage this experimental and evolving technology, entail the use of 7.0T MRI only in research centres with specific projects. In Italy, the introduction of 7.0T MRI in clinical practice will be limited by restrictions of the use of static induction fields exceeding 4 Tesla in the study of the brain.

Future prospects

In future, a better set-up of the hardware and software, new dedicated coils not only for the brain but also for other anatomical districts, self-shielded magnets which allow the use of lighter shielding, may reduce installation and operating costs.

Table 1: Description of the included studies on effectiveness and safety

Study	Inclusion criteria	D	N° (F/M)	Age [years]	Outcomes	Comparator	Conclusion by authors
Cho ZH, 2010	NR	P	1 (F)	48	Structures targeted for deep brain stimulation (DBS)	1.5T and 3.0T	The technology enables the direct visualization of neural structures, could be a valuable aid in neurosurgical procedures.
Ge Y, 2008	Patients with clinically-definite relapsing-remitting MS	MS	2 (F)	54 and 39	Microvascular abnormalities	3.0T	The technology allows for direct evidence of vascular pathogenesis in MS in vivo, with important implications for monitoring lesion activity and therapeutic response.
Kollia K, 2009	Patients with definite MS	MS	12 (4F/8M)	mean 32 (22-47)	Structural abnormalities within MS lesions	1.5T	Better visualization of MS lesions in the gray matter and demonstrated structural abnormalities within the MS lesions themselves more effectively.
Tallantyre EC, 2009	Patients with demyelinating brain disease	MS	7 (4F/3M)	mean 37 (24-48)	Small parenchimal veins	3.0T	More detailed structural anatomy of MS lesions, potential discrimination between MS white matter lesions and microangiopathic lesions.
Tallantyre EC, 2010	Patients with demyelinating disease	MS	11 (7F/4M)	mean 36.6 (24-48)	Cortical lesions	3.0T	Useful for confidently classifying the location of lesions in relation to the cortical/subcortical boundary.

Key: D = Disease; NR = not reported; MS = Multiple Sclerosis; P = Parkinson.

Evidence searches

Searches of EuroScan, CRD (DARE & HTA), Medline, Cochrane Library ed Embase were performed on 12th November 2010.
The search on web site www.clinicaltrial.gov was performed on 14th December 2010.
Combinations of the following keywords were used: *seven-tesla, magnetic resonance, 7 tesla, ultra high field, Parkinson, Alzheimer, Multiple sclerosis, neurodegenerative.*

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Glossary

CRD: Centre for Reviews and Dissemination.

DPR: Decree of the President of the Italian Republic.

FDA: Food and Drug Administration.

Gantry: Place of the device in which the patient is introduced and scanned for the clinical examination.

HS: Horizon Scanning.

ISS: Istituto Superiore di Sanità (Italian National Health Institute).

MRI 8.0T, 7.0T, 3.0T, 1.5T: Magnetic Resonance Imaging 8.0, 7.0, 3.0, 1.5 Tesla.

RDM: Medical device Repertory (http://www.salute.gov.it/dispositivi/paginainternasf.jsp?id=499&menu=repertorio).