

# A comparison of standard laser with micropulse laser for the treatment of diabetic macular oedema

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<b>Registration date</b> 19/05/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 19/10/2023	<b>Condition category</b> Eye Diseases	<input type="checkbox"/> Individual participant data

## Plain English Summary

### Background and study aims

Diabetic retinopathy is the damage of the retina (the light-sensitive tissue lining the back of the eye) caused by diabetes. People with diabetic retinopathy may lose vision as a result of them developing what is called diabetic macular oedema (DMO). DMO is the most common complication of diabetes in the back of the eye. In DMO, fluid leaks in the centre of the retina (macula). The accumulation of this fluid reduces the vision, as the retina needs to be dry to work properly. If the fluid is left untreated, permanent and irreversible visual loss will occur. The amount of fluid in the macula can be measured by doing a scan of the eye called optical coherence tomography (OCT). Depending on the amount of fluid present in the macula, people with DMO will be offered medicines known as anti-vascular endothelial growth factor (anti-VEGF) or laser treatment. The National Institute of Health and Care Excellence (NICE) found that laser treatment was effective in people with DMO and retinas that had been thickened by fluid but below to a certain limit (when the centre of the retina is less than 400 microns in thickness as measured by the OCT) and offers good value for money compared to anti-VEGF injections. Both, standard laser and micropulse laser, are being used currently in ophthalmic clinics across the world. The aim of this study is to compare the effectiveness of these two lasers in the treatment of patients with DMO.

### Who can participate?

Adults who have diabetic retinopathy and DMO.

### What does the study involve?

At the start of the study, all participants have an eye examination and have a sample of blood taken to check their blood sugar control. In addition, their medical history is taken and participants fill in some questionnaires about how they perceive their sight and how their sight may affect their life. Participants are then randomly allocated to one of two groups. Those in the first group are treated with the micropulse laser and those in the second group are treated with the standard laser. The participants do not know which laser they are being treated with. Participants in both groups attend clinic appointments after four, eight, 12, 16, 20 and 24 weeks so that the effects of the treatment can be assessed.

What are the possible benefits and risks of participating?  
There are no direct benefits or risks involved with participating.

Where is the study run from?  
Royal Victoria Hospital, Belfast and 15 other NHS hospitals (UK)

When is the study starting and how long is it expected to run for?  
April 2016 to May 2021

Who is funding the study?  
National Institute for Health Research (UK)

Who is the main contact?  
Ms Lynn Murphy  
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## Contact information

**Type(s)**  
Public

**Contact name**  
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## Additional identifiers

**EudraCT/CTIS number**  
2016-003804-29

**IRAS number**

**ClinicalTrials.gov number**  
NCT03690050

**Secondary identifying numbers**  
CPMS 33318, Protocol number: 16028NL-AF

## Study information

**Scientific Title**

Diabetic Macular Oedema and Diode Subthreshold Micropulse Laser (DIAMONDS): A pragmatic, multicentre, allocation concealed, prospective, randomised, non-inferiority double-masked trial

## **Acronym**

DIAMONDS

## **Study hypothesis**

The aim of this study is to evaluate the clinical effectiveness and cost-effectiveness of Diode Subthreshold Micropulse Laser (DSML), when compared with standard threshold laser, for the treatment of patients with Diabetic Macular Oedema (DMO) with a central retinal subfield thickness of (CST) of < 400 microns.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Office for Research Ethics Committees Northern Ireland- HSC REC A, 17/08/2016, ref: 16/NI/0145

## **Study design**

Randomized; Interventional; Design type: Treatment, Other

## **Primary study design**

Interventional

## **Secondary study design**

Randomised controlled trial

## **Study setting(s)**

Hospital

## **Study type(s)**

Treatment

## **Participant information sheet**

See study outputs table

## **Condition**

Diabetic Macular Oedema

## **Interventions**

Participants are randomised to one of two groups in a 1:1 ratio by an automated randomisation system to generate the random allocation sequence.

Intervention group: Participants undergo treatment with the micropulse laser. This involves the use of a laser technology aimed at minimising damage ("tissue-sparing") to choroid and retina but maintaining treatment efficacy by its selective effect on the retinal pigment epithelium (RPE). It is performed using a laser that, instead of delivering a continuous-wave laser beam, as the standard laser, it provides very small, repetitive, low energy pulses of laser separated by a brief rest period. This rest period allows the tissue to cool down between laser pulses avoiding the increased tissue heat that would be produced by continuous laser and allowing the use of lower laser energy power to achieve an effect. The reduced heat produced in the tissue and the

reduced energy power required for the treatment may reduce side effects. Specifically, the technology does not appear to cause retinal burns or scars associated with decreased retinal sensitivity in treated areas.

**Control group:** Participants receive standard treatment. This involves the use of standard threshold laser with any of the devices used currently for this purpose (e.g. frequency-doubled neodymium-doped yttrium aluminium garnet (Nd:YAG) 532 nm laser, argon laser, diode [561nm or IQ (577nm)] laser. Standard laser is applied to areas of thickened retina, macular non-perfusion and leaking microaneurysms, in accordance the modified ETDRS technique.

At baseline and again after 4, 8, 12, 16, 20, 24 months, participants undergo an ophthalmological examination and OCT scan to establish their eligibility for the study and to determine the changes to their eye following laser treatment. Health and vision related quality of life will be evaluated through the use of the EQ-5D -5L, the NEI VFQ-25 and the VisQoL which will be obtained t baseline and months 12 and 24.

### **Intervention Type**

Procedure/Surgery

### **Primary outcome measure**

BCdVA in the study eye is assessed by a BCdVA test (using ETDRS visual acuity charts at 4 meters) at baseline and months 4,8,12,16,20 and 24.

### **Secondary outcome measures**

1. Binocular BCdVA is assessed by a binocular BCdVA test (using ETDRS visual acuity charts at 4 meters) at baseline and 24 months
2. Central subfield retinal thickness, as determined by spectral domain OCT at baseline and 24 months
3. Mean deviation (MD) of the Humphrey 10-2 visual field is assessed by a Humphrey 10-2 visual field test at baseline, 12 and 24 months
4. Percentage (%) of people meeting driving standards is assessed by an Esterman binocular visual field test at baseline and 24 months
5. Visual functioning (NEI VFQ-25), general health (EQ-5D-5L) and vision and quality of life (VisQoL) are measured using NEI VFQ25, EQ-5D 5L and VisQoL questionnaire scores at baseline and 24 months
6. Incremental cost per quality-adjusted life year (QALY) gained is assessed by a Markov model based cost-utility analysis which will extend beyond the trial analysis period to estimate the longer-term cost-effectiveness, with costs and benefits discounted at 3.5%. The model will be populated by data from the trial and supplemented by estimates of effectiveness, quality of life and costs from published literature and expert opinion.
7. Side effects are measured by a review of the participant's medical and ophthalmic history at 4, 8, 12, 16, 20, 24 months
8. Number of laser treatments needed is assessed by the treating ophthalmologist at 4, 8, 12, 16, 20, 24 months
9. Use of additional treatments (other than laser) is assessed by the treating ophthalmologist at 4, 8, 12, 16, 20, 24 months

### **Overall study start date**

01/04/2016

### **Overall study end date**

## Eligibility

### Participant inclusion criteria

Patients with diabetic retinopathy and centre involving DMO, as determined by using spectral domain optical coherence tomography (SD-OCT), in one or both eyes with:

1. Central retinal subfield thickness of  $> 300$  but  $< 400$  microns as determined by SD-OCT due to diabetic macular oedema

OR

2. Central retinal subfield thickness of  $< 300$  microns provided that intraretinal and/or subretinal fluid is present in the central subfield (central 1 mm) related to diabetic macular oedema

AND

3. Visual acuity of  $> 24$  Early Treatment Diabetic Retinopathy Study (ETDRS) letters (Snellen equivalent  $> 20/320$ )

4. Amenable to laser treatment, as judged by the treating ophthalmologist

5. Over 18 years of age

### Participant type(s)

Patient

### Age group

Adult

### Lower age limit

18 Years

### Sex

Both

### Target number of participants

Planned Sample Size: 266; UK Sample Size: 266

### Total final enrolment

266

### Participant exclusion criteria

Eyes of patients will not be included in the study if:

1. The macular oedema is due to causes other than diabetic macular oedema such as epiretinal membrane, vitreomacular traction, vein occlusion, or others

2. The eye is ineligible for macular laser treatment, as judged by the treating ophthalmologist

3. The eye has DMO and central subfield retinal thickness (CST) of  $> 400$  microns.

4. The eye has active proliferative diabetic retinopathy (PDR) requiring treatment.

5. The eye has received intravitreal Anti- Vascular Endothelial Growth Factor (Anti-VEGF) therapy within the previous two months.

6. The eye has received macular laser treatment within the previous 12 months.

7. The eye has received intravitreal injection of steroids.

8. The eye has received cataract surgery within the previous six weeks

9. The eye has received panretinal photocoagulation within the previous 3 months

The patient:

1. Is on pioglitazone and the drug cannot be stopped 3 months prior to entering into the trial and for the duration of the study
2. Has chronic renal failure requiring dialysis or kidney transplant
3. Has any other condition that in the opinion of the investigator would preclude participation in the study (such as unstable medical status or severe disease that would make it difficult for the patient to be able to complete the study)
4. Has very poor glycemic control and started intensive therapy within the previous 3 months
5. Will use an investigational drug during the study

**Recruitment start date**

18/01/2017

**Recruitment end date**

18/12/2018

## **Locations**

**Countries of recruitment**

England

Northern Ireland

United Kingdom

**Study participating centre**

**Royal Victoria Hospital, Belfast**

Belfast Health & Social Care Trust

Grosvenor Road

Belfast

United Kingdom

BT12 6BA

**Study participating centre**

**Moorfields Eye Hospital**

162 City Road

London

United Kingdom

EC1V 2PD

**Study participating centre**

**The John Radcliffe Hospital**

Oxford Eye Hospital

Headley Way

Oxford

United Kingdom  
EC1V 2PD

**Study participating centre**  
**Manchester Royal Eye Hospital**  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**  
**Sunderland Eye Infirmary**  
Queen Alexandra Road  
Sunderland  
United Kingdom  
SR2 9HP

**Study participating centre**  
**Freeman Hospital**  
Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Study participating centre**  
**Bristol Eye Hospital**  
Lower Maudlin Street  
Bristol  
United Kingdom  
BS1 2LX

**Study participating centre**  
**Frimley Park Hospital**  
Portsmouth Road  
Frimley  
United Kingdom  
GU16 7UJ

**Study participating centre**  
**Royal Hallamshire Hospital**  
Directorate of Ophthalmology  
Glossford Road  
Sheffield  
United Kingdom  
S10 23F

**Study participating centre**  
**King's College Hospital**  
Normandy Building  
Denmark Hill  
London  
United Kingdom  
SE5 9RS

**Study participating centre**  
**Hinchingbrooke Hospital**  
Hinchingbrooke Park  
Hinchingbrooke  
Huntingdon  
United Kingdom  
PE29 6NT

**Study participating centre**  
**Bradford Teaching Hospitals**  
Bradford Royal Infirmary  
Duckworth Lane  
Bradford  
United Kingdom  
BD9 6RJ

**Study participating centre**  
**James Cook University Hospital**  
Marton Road  
Middlesbrough  
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TS4 3BW

**Study participating centre**



**Hull and East Yorkshire NHS Trust**  
Anlaby Road  
Hull  
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HU3 2JZ

**Study participating centre**  
**Stoke Mandeville Hospital**  
Aylesbury  
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HP21 8AL

**Study participating centre**  
**Hillingdon Hospital**  
Pield Heath Road  
Uxbridge  
United Kingdom  
UB8 3NN

## **Sponsor information**

### **Organisation**

Belfast Health & Social Care Trust

### **Sponsor details**

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### **Sponsor type**

Hospital/treatment centre

### **ROR**

<https://ror.org/02tdmfk69>

# Funder(s)

## Funder type

Government

## Funder Name

National Institute for Health Research

## Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

## Funding Body Type

Government organisation

## Funding Body Subtype

National government

## Location

United Kingdom

# Results and Publications

## Publication and dissemination plan

The final study report will be provided by the Trial Statistician. It is anticipated that the study findings will be published in national and international peer review journals and these articles will be led by the CI. This will secure a searchable compendium of these publications and make the results readily accessible to the public and health care professionals. In addition, study findings may be presented at both national and international meetings and to appropriate patient groups.

A report containing the methodology and results of this randomised trial will be published as a Health Technology Assessment monograph, freely accessible via the NIHR HTA webpage. The Royal College of Ophthalmologist will be contacted once the study is completed to allow the trials findings to be incorporated in future Diabetic Retinopathy guidelines.

## Intention to publish date

28/02/2023

## Individual participant data (IPD) sharing plan

Current individual participant data (IPD) sharing statement as of 30/05/2022:

The datasets generated and/or analysed during the current study will be available upon request following the publication of the primary and secondary outcomes. Formal requests for data should be made in writing to Prof. Noemi Lois (Chief Investigator) via the NICTU (info@nictu.hscni.net). Requests will be reviewed on a case by case basis in collaboration with the Sponsor.

Previous individual participant data (IPD) sharing statement:

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository the MACRO Database (<https://nictu.hscni.net/Macro/>)

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Participant information sheet</a>	version V3	29/11/2016	19/05/2017	No	Yes
<a href="#">Protocol article</a>	protocol	12/02/2019		Yes	No
<a href="#">Results article</a>		01/12/2022	06/02/2023	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Cost-effectiveness analysis	18/10/2023	19/10/2023	Yes	No