Utilising optical coherence tomography measures as surrogates for raised intracranial pressure in idiopathic intracranial hypertension

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Express summary

Can optical coherence tomography of papilledema predict intracranial pressure in idiopathic intracranial hypertension?

Findings

This two stage analysis of 104 participants' optic nerve head volume measures of central thickness, central volume, maximum height (any point) and maximum height (central slice) all correlated with ICP either measured by telemetry or by lumbar puncture. Macular ganglion cell layer volume also correlated with visual field mean deviation at 12-months.

Meaning

Optical coherence tomography imaging has the potential to be a non-invasive measure of ICP. The central thickness values were able to predict treatment effect (change in intracranial pressure) at 12- and 24-months.

Background

There is an unmet need for non-invasive biomarkers of intracranial pressure (ICP). ICP manifests as papilledema which can be quantified by optical coherence tomography (OCT) imaging. The objective of this study was to determine whether OCT of the optic nerve head in papilledema could act as a surrogate measure of ICP.

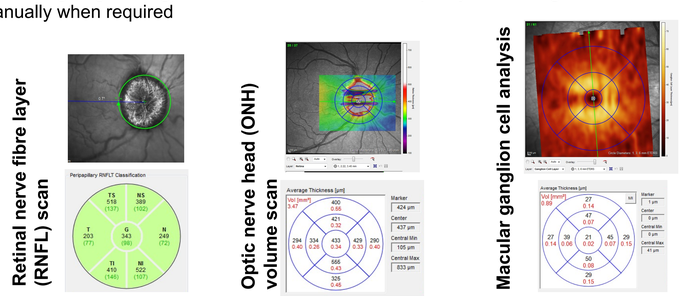
Study design

This is a longitudinal cohort study using data collected from three randomised controlled trials, between from April 1st, 2014 to August, 1st 2019. OCT imaging and automated perimetry was followed immediately by ICP measurement on the same day. Cohort 1 utilised continuous sitting telemetric ICP monitoring (Raumedic Neurovent P-tel device) on one visit. Cohort 2 were evaluated at baseline, 3, 12 and 24 months and underwent lumbar puncture assessment of ICP.

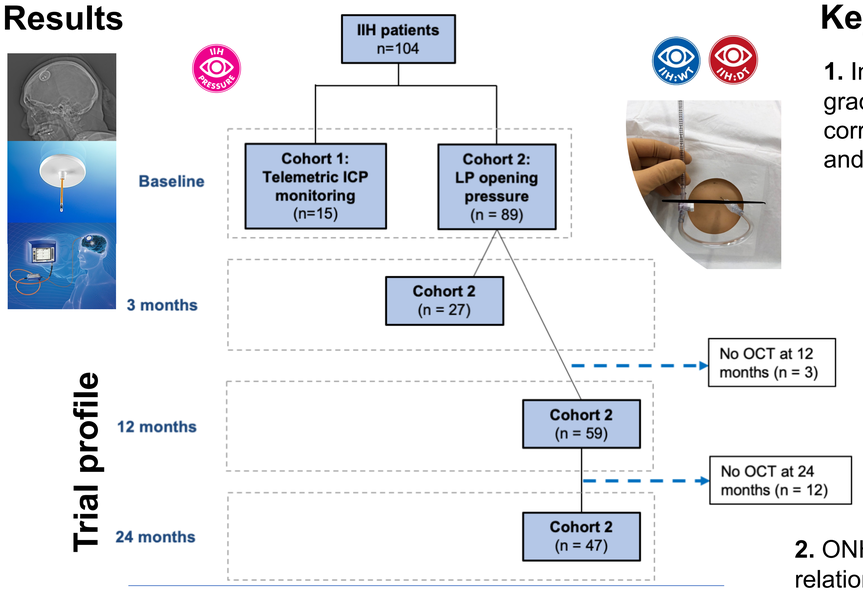
104 participants with active Idiopathic Intracranial Hypertension were enrolled from five National Health Service hospitals in the United Kingdom.

Main outcome measures

OCT measures of the optic nerve head and macula were correlated with ICP, Frisén grading and perimetric mean deviation. The OCT protocol included peripapillary retinal nerve fibre layer, optic nerve head and macular volume scans (SPECTRALIS™, Heidelberg Engineering). All scans were validated for quality and re-segmented manually when required



Results



Age, BMI, ICP and OCT measurements are described by mean ± standard deviation; visual field MD is reported as median (range).

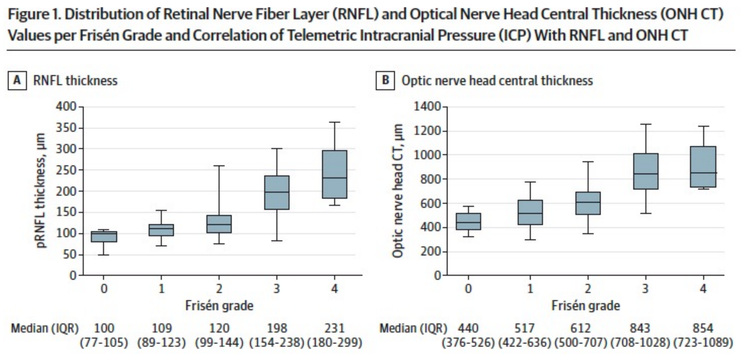
aICP measurements have been made comparable by converting the cohort 1 supine mmHg to cmH20. GCL, ganglion cell layer; RNFL, peripapillary retinal nerve fibre layer thickness; ONH, optic nerve head.

Baseline characteristics

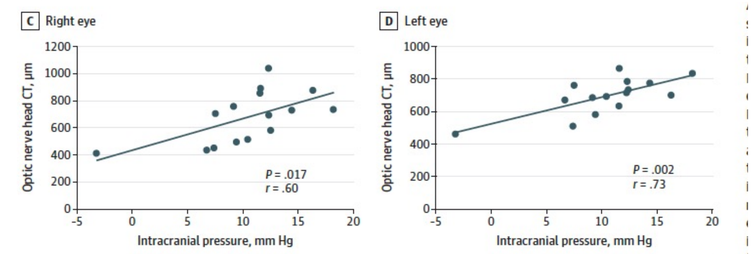
	All (n = 104)	Cohort 1 (telemetric ICP; n = 15)	Cohort 2 (lumbar puncture; n = 89)
Age (years)	31.3 ± 7.9	28.2 ± 9.4	31.8 ± 7.5
Body Mass Index (kg/m^2)	42.1 ± 9.2	38.1 ± 6.2	42.7 ± 9.5
Mean deviation (dB)	-1.88 (-24.76, 6.9)	-0.89 (-5.66, 4.47)	-2.0 (-24.76, 6.9)
Intracranial pressure (cmH_20)	33.6 ± 4.9[a]	29.9 ± 6.7[a]	34.2 ± 5.6
RNFL thickness (µm)	137 ± 57	166 ± 80	133 ± 53
ONH central thickness (µm)	650 ± 196	731 ± 144	634 ± 203
Macular GGL global volume (mm^3)	1.1 ± 0.1	1.09 ± 0.1	1.1 ± 0.1

Key Findings

1. Initially the relationship between papilledema severity, according to Frisén grading, to the OCT parameters and mean deviation were analysed. A strong correlation between Frisén grading and both the RNFL ($p < 0.0001$; $r = 0.4655$) and ONH CT ($p < 0.0001$; $r = 0.5728$) was noted.

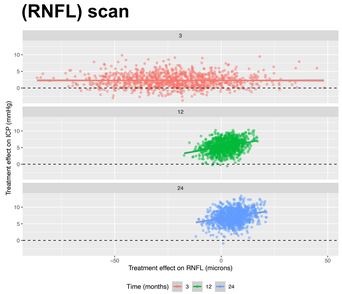


2. ONH CT was chosen pragmatically as this was a whole integer, to evaluate the relationship with ICP in cohort 2 (a larger cohort with ICP measured using LP). ICP correlated with ONH CT with increasing strength over disease duration (baseline, 12 and 24 months).

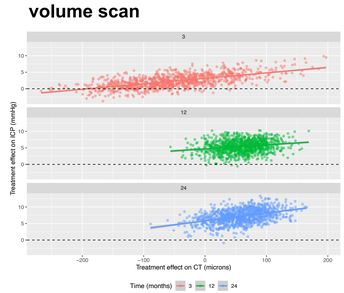


3. Surrogacy analysis identified a positive association between ICP and ONH CT at 3, 12 and 24 months, with a larger treatment effect for CT coinciding with a larger treatment effect for ICP.

Retinal nerve fibre layer (RNFL) scan



Optic nerve head (ONH) volume scan



Predication of change in ICP from OCT ONH central thickness

Time (mths)	Change in optic nerve head volume central thickness measure (µm)	Change in mean intracranial pressure (cmCSF) (95% confidence interval)
12	50	5.0 (1.4 – 8.3)
12	100	5.9 (1.9 – 9.1)
24	50	6.5 (2.3 - 9.9)
24	100	8.5 (4.8 – 12.6)

OCT optic nerve head volume measures (particularly central thickness) reproducibly correlates with ICP and surrogacy analysis demonstrates its ability to inform ICP changes. Our data suggests that it has the utility to not only monitor papilledema but also non-invasively predict ICP in Idiopathic Intracranial Hypertension.