The IONDT, it is appropriate to consider to what extent nased new-onset NAION, randomizing them between op-
tume. The IONDT studied patients with clinically diag-
iing whether the procedure was truly efficacious, ini-
tation of NAION cases, and it was only the progressing
worse, there is no treatment established to be effective.
progressive NAION.

Thus, it can be understood why there was so much hope
improvement after optic nerve sheath decompression. Patients
The pathophysiology of NAION remains a mystery, and

cause a new study to have an 80% probability of detecting
in the older population, is a peculiar dis-
neuropathy (NAION), the most com-
ONARTERITIC ANTERIOR ISCHEMIC OPTIC
neuropathy (NAION), the most com-
order. It has a predilection for eyes with
very small cup-disc ratios, causes predominantly infer-
rior altitudinal visual field defects, and, like Thor’s ham-
erarely strikes the same eye twice. Vision is lost rap-
ly, usually within days. However, in a small fraction
of patients, visual acuity or field worsens over weeks, ie,
“progressive NAION.”

The results of the IONDT have influenced the manage-
ment of patients with NAION. At first glance, it would
seem that the IONDT conclusively showed that optic
nerve sheath fenestration does not improve visual acu-
it in patients with NAION and may also be harmful. How-
ever, a closer analysis uncovers some ambiguity. First,
the IONDT did not definitively answer whether fenes-
tration helped the group of patients for which the therapy
was originally described: namely, those with progres-
severe NAION. The 1989 article describing optic nerve
sheath fenestration for progressive NAION had spec-
cifically demonstrated that it was ineffective for nonpro-
gressive NAION. The IONDT was underpowered to spe-
cifically assess progressive NAION, and the negative
findings seen in both progressing and nonprogressing
cases has made it unlikely that a more adequately pow-
ered study can be performed in the future. Of the 237
randomized patients in the IONDT, only 16 patients in
the surgery group and 11 patients in the follow-up group
could be considered progressive by 1 clinical criterion,
namely, worsening of 3 or more lines of visual acuity be-
fore randomization. In comparison, if one were to de-
sign a new study to have a 50% greater improvement of 3 lines or
more beyond that found in the IONDT careful fol-
day, 66 patients per group would be required.

More than a decade after publication of the results of the
IONDT,2 it is appropriate to consider to what extent

Lessons From the Ischemic Optic Neuropathy Decompression Trial

A Decade Later

Leonard A. Levin, MD, PhD

N

Author Affiliations: Department of Ophthalmology and Visual
Sciences, University of Wisconsin Medical School, Madison; and
Department of Ophthalmology, University of Montreal, Montreal,
Quebec, Canada.

improve the progressive form of nonarteritic ischemic optic neuropathy. Arch
11. Kelman SE, Elman MJ. Optic nerve sheath decompression for nonarteritic is-
chemic optic neuropathy improves multiple visual function parameters. Arch
12. Spoor TC, Wilkinson MJ, Ramocki JM. Optic nerve sheath decompression for
the treatment of progressive nonarteritic ischemic optic neuropathy. Am J
13. Spoor TC, McHenry JG, Lau-Sickon L. Progressive and static nonarteritic is-
chemic optic neuropathy treated by optic nerve sheath decompression. Ophthalmology.
14. Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve
decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION)
is not effective and may be harmful. JAMA. 1995;273(8):625-632.
15. Ischemic Optic Neuropathy Decompression Trial Research Group. Ischemic Op-
16. Feldon SE. Computerized expert system for evaluation of automated visual fields from
the ischemic optic neuropathy decompression trial: methods, baseline fields, and six-
17. Crawley B, Scherer R, Langenberg P, Dickersin K. Participation in the Ischemic
Optic Neuropathy Decompression Trial: sex, race, and age. Ophthalmic Epidemiol.
18. Ischemic Optic Neuropathy Decompression Trial Research Group. The Ische-
ic Optic Neuropathy Decompression Trial (IONDT): design and methods. Con-
19. Feldon SE, Scherer RW, Hooper FJ, et al. Surgical quality assurance in the Is-
chemic Optic Neuropathy Decompression Trial (IONDT). Control Clin Trials. 2000;
24(3):294-305.
not have achieved the surgical facility that comes with high-volume procedures. Recognizing these potential problems, the IONDT investigators went to heroic lengths to attempt surgical uniformity, including the use of questionnaires and a videotape of a fenestration operation by each study surgeon. The investigators deserve to be lauded for employing these measures. However, it is never easy to navigate between the Scylla of achieving an adequate head count in a clinical trial and the Charybdis of using data pooled from surgeons among whom skill and experience vary. Feldon and colleagues described the surgical quality-assurance methods used in the IONDT. It is clear that even within this group of experienced surgeons there were great differences in their surgical technique, including the failure to adhere to 4 of the 6 required steps in the protocol for optic nerve decompression surgery in up to 20% of centers. The other 2 required steps mandated that intervals of sustained traction on the globe be limited to 7 minutes interspersed with at least 2 minutes of “rest.” Not only was compliance difficult to assess, but it is possible that even 7 minutes of greatly elevated intraocular pressure was harmful, and this could have been 1 of the factors contributing to the worse visual outcome in the surgical arm of the IONDT.

Given these questions, how has clinical practice changed because of the IONDT? It showed that optic nerve sheath fenestration for nonprogressive NAION in the hands of most surgeons is not helpful, and thus the trial stopped an epidemic of ineffective and possibly dangerous surgery. This in itself completely changed the treatment of NAION. In addition, as reflected in an impressive list of articles published from the IONDT, our knowledge of the clinical features and natural history of the disease has been greatly expanded. The character of the visual field defects, the appearance of the optic disk, and many other elements are now better known because the trial enrolled a rigorously selected patient population who were evaluated in a uniform fashion. Based on the results of the IONDT, every ophthalmologist should know that 43% of patients with NAION experience a spontaneous improvement of at least 3 lines of visual acuity at 6 months. Although it is unclear whether improvement reflects true healing or simply improved scanning strategies, an ophthalmologist armed with this information can offer some hope to NAION patients who are overwhelmed by unexpected visual loss from an as yet untreatable disease. Meanwhile, the search for effective therapies continues.

Submitted for Publication: October 17, 2006; final revision received December 12, 2006; accepted December 19, 2006.

Correspondence: Leonard A. Levin, MD, PhD, Department of Ophthalmology and Visual Sciences, University of Wisconsin Medical School, 600 Highland Ave, Madison, WI 53792 (lalevin@facstaff.wisc.edu).

Financial Disclosure: Dr Levin is, or has been in the past 5 years, a consultant on neuroprotection for Alcon Laboratories Inc, Allergan Inc, Fovea Pharmaceuticals SA, Merck and Co Inc, Pfizer Inc, and Santen Pharmaceutical Co Ltd.

REFERENCES

2. Ischemic Optic Neuropathy Decompression Trial Research Group. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. JAMA. 1995;273(8):625-632.

From the Archives of the Archives

In view of the great wealth of this century and the strong appeal made by blindness, it is remarkable how little has been donated to ophthalmic hospitals and for ophthalmic research. The Wilmer Institute, opened in 1924, and the Howe Laboratory of Ophthalmology, organized in 1931, were the first institutions in America especially endowed for ophthalmic research, and their endowments are still relatively inadequate. Now that government is preventing the accumulation of great private wealth, it may take over the financing of many institutions formerly largely dependent on private donations. That this is a desirable consummation is questionable.