Childhood Intermittent Exotropia

Intermittent Exotropia (IXT)

**What We Know**
- Most common form of childhood-onset XT
- Normal alignment & sensory fusion sometimes
- Good stereoacuity at near (generally)
- Amblyopia is rare

**What We Don’t Know**
- Natural history
- Best form of treatment

Course Objectives: PEDIG Findings
- IXT treatment based on randomized clinical trials
  - Overminus lenses
  - Part-time patching
  - Surgery
- Natural history of IXT based on 3-year observational study
- Define / describe outcome measures

Outcome Measure for Studies of IXT?
- What Should We Measure?
  - Magnitude?
  - Stereoaucuity?
  - % Time of Alignment

Outcome Measure for Studies of IXT?
- Control of IXT
  - % Time of Alignment or Frequency

Financial Disclosures
- No financial interest in materials or methods discussed herein
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Ways of Assessing Control of IXT

- Patient and parental report
- Cover testing
  - Proportion of time XT is manifest
  - Speed of recovery - see video
- PEDIG IXT control scale

PEDIG IXT Control Scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Constant XT</td>
</tr>
<tr>
<td>4</td>
<td>XT &gt;50% of time</td>
</tr>
<tr>
<td>3</td>
<td>XT &lt;50% of time</td>
</tr>
<tr>
<td>2</td>
<td>&gt; 5 seconds to recover</td>
</tr>
<tr>
<td>1</td>
<td>1-5 seconds to recover</td>
</tr>
<tr>
<td>0</td>
<td>&lt; 1 second to recover</td>
</tr>
</tbody>
</table>

Control of XT: Start at Distance

Step 1: 30 sec observation before dissociation at distance

- No spontaneous tropia at near
- Control score must be <3
- (so...must dissociate at near)

Control of XT: Near

Step 2: Near - 30 second observation before dissociation

- No spontaneous tropia at near

Dissociate (occlude) for 10 sec; Uncover & observe recovery 3X: OD, OS, Worst eye

- NOTE: If recovery >5 seconds for OD, control score = 2
  & no further testing needed
**Dissociate (occlude) for 10 sec; Uncover & observe recovery 3X: OD, OS, Worst eye**

1 2 3 4 5 6

Near Control = 2

NOTE: If recovery >5 seconds for OD, control score = 2 & no further testing needed

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**PEDIG IXT Control Scale**

<table>
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</table>

Distance Control = 3
Near Control = 2

Mohney BG, Mahoney M. Strabismus 2006;14(3):147-150

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**Outcome Measure for PEDIG IXT Studies**

PEDIG IXT Control Scale

% Time of Alignment
- At present, taking the mean of 3 measures during exam vs. using a single measure*
- Better represents overall control than single measure


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**Cover Testing: Clinical Tip**

Test distance at far can make a difference
Use remote test distance

<table>
<thead>
<tr>
<th>Divergence Excess XT</th>
<th>3m vs. 6m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased angle 5-15Δ</td>
<td>64%</td>
</tr>
<tr>
<td>Surgery (yes/no)</td>
<td>32%</td>
</tr>
<tr>
<td>Surgical dose different</td>
<td>32%</td>
</tr>
</tbody>
</table>

Samantha: IAXT (50%) 14Δ at 3m; CAXT 25Δ at 50ft


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**Evidence in Relation to Treatment of Childhood IXT PEDIG RCT’s**

- Part-time Patching
  - RCT: Patching vs Observation
    - 3 to <11 years
    - 12 to 35 months

- Overminus Lenses
  - RCT: Over-minus vs Observation
    - 3 to <7 years

- Surgical Procedure
  - RCT: Bil LR Recession vs Unilateral Recess-Resect for Basic IXT
    - 3 to <11 years

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**PEDIG RCT’s**
Effectiveness of part-time patching in reducing risk of deterioration of IXT over 6 months?

IXT: Part-time Patching Background

- Reported benefits
  - Eliminates suppression
  - Reduces magnitude +/- or frequency
  - Changes character of deviation
- Commonly prescribed by peds ophthalmology
  - Varying dosages, duration, outcomes
  - Retrospective, small samples, no comparison group

Intermittent Exotropia-2 (IXT-2)
RCT’s Comparing Part-time Patching with Observation for Children with IXT

Study Objective

- Determine effectiveness of prescribed part-time patching for reducing risk of deterioration of IXT over 6 months among children:
  - 3 to <11 years old
  - 12 to 35 months old

Major Eligibility Criteria

- Age: 3 to <11 years; 12 months to 35 months
- Previously untreated IXT (any type)
  - IXT or CXT at distance; & IXT or XP at near
  - $\geq 10^\circ$ at distance
  - $\geq 15^\circ$ at distance +/- or near
- Near stereoacuity of 400" (only older cohort)
- No amblyopia or amblyopia treatment in last year
- Investigator / child / parent willing forgo all other IXT treatment until deterioration criteria met

IXT-2 Study Overview

Previously Untreated Children with IXT
Younger: 12 to 35 months
Older: 3 to <11 years

Observation
(Rx if needed)
3-months
6-month Primary Outcome

Patching
3 hours / day
3-months
6-month Primary Outcome
**IXT-2 Study Overview**

- Randomized
- Previously Untreated IXT

- Observation
  - Masked assessment (deterioration criteria met)
- Patching
  - 3 hrs/day

- 3-month Primary Outcome
- 6-month Primary Outcome

* Masked examiner with retest
* *1* month wash out; stop patching at 5 months

**Primary Outcome: Deterioration by 6 Months**

Formal Deterioration Criteria:
- Constant XT ≥10∆ at Dist & Near* or
- Near stereopsis: drop ≥ 2 octaves from baseline*

- **Baseline Stereo arc sec**
- Stereo at FU visit to meet deterioration*
  - 40 200 or worse
  - 60 400 or worse
  - 100 800 or worse
  - 400 Nil

**Also Considered Deterioration**

If non-protocol treatment started without meeting formal deterioration criteria:
1. And no allowed exceptions
2. Even if allowed exceptions of:
   - Debilitating diplopia
   - Overwhelming social concern (parent/child)
   - Failure to keep up with stereo age norms

**Part-Time Patching Results?**

3 to <10 year olds

**Deterioration by 6 Months Was Uncommon**

<table>
<thead>
<tr>
<th></th>
<th>Observation</th>
<th>Patching</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deteriorated</td>
<td>6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Not Deteriorated</td>
<td>94%</td>
<td>99.4%</td>
</tr>
</tbody>
</table>

- Difference in proportions = 5.4%
- Lower limit of 1-sided exact 95% CI = 2.0%; P = 0.003


**3 to <10 Years**

Small Difference in Deterioration By 6 Months

<table>
<thead>
<tr>
<th>Deterioration by 6 Months</th>
<th>Observation (N=165)</th>
<th>Patching (N=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) Deteriorated</td>
<td>6 (4.8%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Formal deterioration criteria met</td>
<td>7 (4.2%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Constant XT ≥10∆ D&amp;N</td>
<td>1 (0.6%)**</td>
<td>0</td>
</tr>
<tr>
<td>Stereo worsened ≥ 2 octaves</td>
<td>6 (3.6%)</td>
<td>1 (0.6%)</td>
</tr>
<tr>
<td>Both criteria</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Started treatment against protocol</td>
<td>3 (1.8%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Number (%) Deteriorated**

- Difference in proportions = 5.4%; Lower limit of 1-sided exact 95% CI = 2.0%; P = 0.003
### Part-Time Patching

#### Take Home Message

- Deterioration of IXT over 6 months was uncommon.
- 3 to <11 yrs: Observation or PT-patching both reasonable management approaches.
- 12 to 35 mo: Insufficient evidence to recommend PT patching.

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### Overminus Lens Therapy for IXT

#### What We Know
- "What We Don’t Know"
Overminus Lens Therapy for IXT

- Rx more minus (or less plus) than distance refraction
- Mechanism?
  - Magnitude reduced by stimulating A/C
  - A/C triggers reflex fusional vergence
  - May allow clear distance vision, facilitating fusion
- Stimulation of accommodation by:
  - Excessive convergence required for fusion (convergence accommodation)?
  - Reliance on excessive AC to overcome XT?

Intermittent Exotropia Study 3 (IXT3)

A Pilot Randomized Clinical Trial of Overminus Spectacle Therapy for Intermittent Exotropia

Major Eligibility Criteria

- Age: 3 to <7 years
- IXT
  - Distance control score ≥ 2 (mean of 3)
  - Near control score ≠ 5 (mean of 3)
  - ≥ 15° exo at distance by PACT
  - Near not exceed distance by >10 Δ (PACT)
- SE between +1.00 D and -6.00 D OD & OS

Intermittent Exotropia Study-3: Study Objective

Assess initial short-term response of IXT to overminus lenses

IXT-3 Study: 3 to <7 Years

Baseline XT Control at Distance

<table>
<thead>
<tr>
<th>Control Score</th>
<th>Observation (N=31) Mean = 3.2</th>
<th>Overminus (N=27) Mean = 3.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to &lt; 1</td>
<td>42%</td>
<td>35%</td>
</tr>
<tr>
<td>1 to &lt; 2</td>
<td>44%</td>
<td>39%</td>
</tr>
<tr>
<td>2 to &lt; 3</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>3 to &lt; 4</td>
<td>22%</td>
<td>21%</td>
</tr>
<tr>
<td>4 to 5</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Over-Minus Lenses Results?

Overminus Group Had Better Mean Distance Control at 8 Weeks

Overminus Lenses for 3 to <7 Year Old Children With IXT

Take Home Message

Improved distance control at 8 weeks
Larger & longer RCT needed to assess effectiveness of overminus lenses on and off treatment

Currently Recruiting

Intermittent Exotropia Study 5 (IXT-5)

RCT of Overminus Spectacle Therapy for IXT

Currently Recruiting:
12 months on treatment, then wean off treatment

Overminus Lens Tx: Cotter Clinical Impressions

- Patient profile
  - Age?
  - Accommodative function?
  - AC/A ratio? (Basic or DE; not CI)
- Determination of overminus power?
  - Decrease in IXT magnitude?
  - Decrease in IXT frequency? Look for improvement in this--
  - What if results in eso at near? Rx a bifocal

Baseline XT Control at Near

Percentage of Patients

0% 10% 20% 30% 40% 50% 60%
0 to <1 1 to <2 2 to <3 3 to <4 4 to 5

Observation (N=31) Mean = 1.5
Overminus (N=27) Mean = 1.3

Overminus Group Had Better
Mean Distance Control at 8 Weeks

Difference = 0.80 (1.49 to -0.11)
P = 0.01 for one-sided test

Mean 8-week Distance Control

2.8 points
2.0 points

Observation
Over-minus


Overminus Lens Therapy

- Length of treatment?
- Parental education – very important
- Myopia progression: no evidence of this yet
  - Retrospective chart reviews

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial RE</th>
<th>Change After 5 Y</th>
<th>Change After 10 Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (62)</td>
<td>0.00 ± 1.40</td>
<td>-1.40 ± 2.00</td>
<td>-2.41 ± 2.20</td>
</tr>
<tr>
<td>6-mo Tx (74)</td>
<td>0.00 ± 1.50</td>
<td>-1.52 ± 1.80</td>
<td>-2.34 ± 2.40</td>
</tr>
<tr>
<td>5-yr Tx (34)</td>
<td>-0.10 ± 1.50</td>
<td>-1.54 ± 1.90</td>
<td>-2.36 ± 2.10</td>
</tr>
</tbody>
</table>


Natural History of IXT in Children?

For Example: Surgery - Balance of Possibilities

☑ Improvement of social concerns
☑ Possibility of improving distance & retaining near stereoacuity
☑ Possibility of spontaneous improvement
☑ Surgical complications & high rate of reoperations
☑ Possibility of loss of stereoacuity through surgical overcorrection*

Pros

Cons

*21% overcorrection 6-mo post surgery; Buck et al. BMC Ophthalmology 2012

IXT-2 Study Overview

Randomized

Observation: No Treatment

3-Months

6-Month

Outcome for RCT

12, 18, 24, 30 month FU Visits

36 months: Natural History Outcome

Patching

Masked Examinations
  ▪ Ocular alignment
  ▪ Stereoacuity
  ▪ XT control

12, 18, 24, 30 month FU Visits

36 months - Study Completed

Baseline IXT Characteristics

- 183 children randomized to observation
- 83% completed the study
- Mean age = 6.1 years
- 63% female; 61% white
- 40-60 arc sec stereo at near: 62%
- Type of IXT: 69% basic exo; 21% pseudo-DE

Natural History of IXT in Young Children

Objective

Deterioration of IXT Over 3-Year Period in Children with Untreated IXT Ages 3 to 10 Years Old

PEDIG. Unpublished data
Primary Outcome - Deterioration by 3 Years

- Unpublished data presented
- Abstract available


Natural History of IXT in Young Children

Deterioration of IXT Over 3-Year Period in Children with Untreated IXT Ages 12 to 35-Month Old Children

Unpublished data

Study Objective

• Determine long term effectiveness of BLRc (bilateral lateral rectus recession) vs. R/R (unilateral lateral rectus recession with medial rectus resection) for treatment of basic type and pseudo-DE type IXT

Table 2: Surgical Dose

<table>
<thead>
<tr>
<th>Angle of Largest Deviation by PACT</th>
<th>Lateral Rectus (LR)*</th>
<th>Medial Rectus (MR)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>16 PD</td>
<td>4.0 mm</td>
<td>3.0 mm</td>
</tr>
<tr>
<td>18 PD</td>
<td>5.0 mm</td>
<td>4.0 mm</td>
</tr>
<tr>
<td>20 PD</td>
<td>5.0 mm</td>
<td>4.0 mm</td>
</tr>
<tr>
<td>25 PD</td>
<td>6.0 mm</td>
<td>5.0 mm</td>
</tr>
<tr>
<td>30 PD</td>
<td>7.0 mm</td>
<td>5.5 mm</td>
</tr>
<tr>
<td>35 PD</td>
<td>7.5 mm</td>
<td>6.0 mm</td>
</tr>
<tr>
<td>40 PD</td>
<td>8.0 mm</td>
<td>6.5 mm</td>
</tr>
<tr>
<td>45 PD</td>
<td>8.5 mm</td>
<td>6.5 mm</td>
</tr>
<tr>
<td>50 PD</td>
<td>9.0 mm</td>
<td>7.0 mm</td>
</tr>
</tbody>
</table>

Primary Outcome

Suboptimal Surgical Outcome BY 3 Years

• Suboptimal surgical outcome criteria (exotropia, constant ET or stereo loss) met at ANY visit

OR

• Reoperation without meeting suboptimal surgical outcome criteria

Abstract found at:
Chen AM, Cotter SA, Chandler DL, Holmes JM, Donahue SP, on behalf of PEDIG. “A Randomized Trial Comparing Bilateral Lateral Rectus Recession versus Unilateral Recess-Resect for Basic Type Intermittent Exotropia.” Optometry and Vision Science 2017; 93: E-abstract 175227

Treatments for IXT

• Monitor; watchful waiting
  ✓ Part-time patching
  ✓ Over-minus lenses
  ✓ BI Prism
  ✓ Vision therapy
  ✓ Surgery

Thank You

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