

# Liquid Nitrogen (N<sub>2</sub>O) Cryotherapy (N<sub>2</sub>OCryo) for Cervical Intraepithelial Neoplasia (CIN)

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## Introduction

In general, the patients with ASCUS/LSIL cytology would be follow-up with the interval of three or six months. However, we performed N<sub>2</sub>O cryotherapy (N<sub>2</sub>OCryo) to improve abnormal cytology for the patients with SIL/CIN.

## Materials and Methods

Between April 2015 to September 2019, retrospectively we analyzed patients with abnormal cytology of ASC-US/LSIL into the groups: A group of 47 cases with just follow-up without any treatment, B group of 45 cases with N<sub>2</sub>OCryo according to colposcopic and/or cytological abnormality and HPV infection.

Furthermore, 31 patients with HSIL undergone N<sub>2</sub>OCryo were also compared to the effectiveness of clearance of abnormal cytology and HPV infection. Patients performed N<sub>2</sub>OCryo three times every four weeks with written informed consent.

## Treatment schedule of N<sub>2</sub>O cryotherapy

At our outpatient clinic after the diagnosis of SIL/CIN, under the written informed consent, N<sub>2</sub>OCryo was performed within less than thirty seconds every month three times (Fig. 1). Patients felt some coldness without pain and watery discharge for a week. Then response was evaluated with colposcopy, cervical cytology and HPV test. Complete response (CR) was defined with cytology NILM and HPV negative, partial response (PR) with any mild abnormal cytology or HPV positive, no change (NC) with persistent cytology and/or HPV infection and progressive disease (PD). After the evaluation N<sub>2</sub>OCryo, we continued the follow-up with the interval of 3 or 6 months by using cytology and/or HPV test with call/recall system for several years.

## Results

Table 1. Effectiveness of N<sub>2</sub>O Cryotherapy

	ASC-US/LSIL A group	ASC-US/LSIL B group	ASC-H/HSIL C group
Cases	47	45	31
CR NILM&HPV-	4	14	9
PR Cytol- or HPV-	14	14	12
NC (no change)	10	10	6
PD (grade-up)	1	1	
Drop out	3	1	1
Ongoing		5	3
No visit for check	15	0	0
Response rate(CR,PR)	18(4,14)/47 38.3%	28(14,14)/45 62.2%	21(9,12)/31 67.7%
Only evaluable cases	18/29 62.1%	28/40 70.0%	21/27 77.8%

2019.9.30 at present

Fig.1

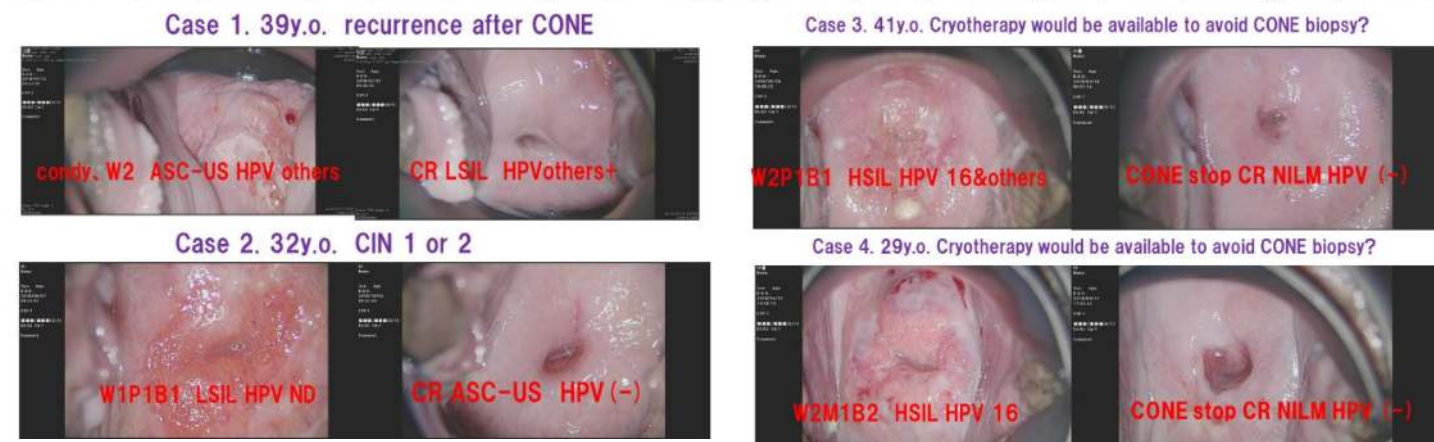


## Effectiveness of N<sub>2</sub>O cryotherapy (Table 1)

A group (ASC-US/LSIL) followed by observation with 47 cases showed 4CR, 14PR, 10NC, 1 PD, and 15 no visit for check. Response rate (CR,PR) was 38.3% in total and 62.1% among 29 response evaluable cases. B group (ASC-US/LSIL) treated by N<sub>2</sub>OCryo with 45 cases showed 14 CR, 14 PR, 10 NC, 1 PD. Response rate (CR,PR) was 62.2% in total and 70.0% among 40 response evaluable cases (Fig. 2). C group (ASC-H/HSIL) treated by N<sub>2</sub>OCryo with 31 cases showed 9 CR, 12 PR, 6 NC. Response rate (CR,PR) was 67.7% in total and 77.8% among 27 response evaluable cases (Fig. 3).

We suspect ASC-US/LSIL is temporarily infectious disease and spontaneously regressed, rarely progressed. ASC-H/HSIL is persistent or progressed but rarely regressed, then N<sub>2</sub>OCryo is meaningful for prevent the cone biopsy.

Fig. 2. Colposcopic findings of pre- & post- N<sub>2</sub>O Cryotherapy Fig. 3. Colposcopic findings of pre- & post- N<sub>2</sub>O Cryotherapy



## Changes of colposcopic findings, Cytology, HPV status after N<sub>2</sub>O Cryotherapy (Table 2)

Table 2. Abnormal findings before & after N<sub>2</sub>O cryotherapy

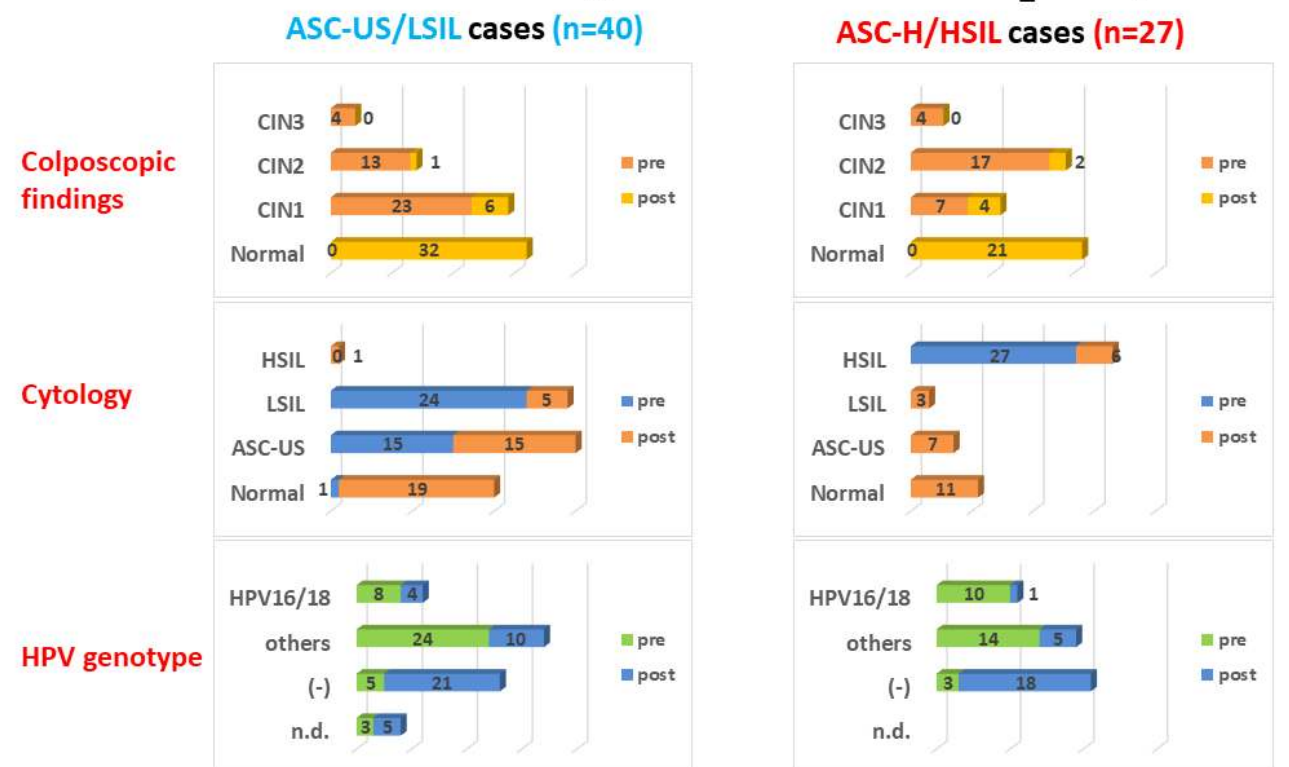


Table 3. Follow-up after N<sub>2</sub>O cryotherapy

ASC-US/LSIL cases after NC (n=39)					
Follow-up	CR cases	14	no recurrence		6-48 months
&	PR cases	14	NC add. 1	CONE 1 TLH 1	6-44 months
Add. Tx	NC cases	10	NC add.4	CONE 1	6-24 months
	PD cases	1		CONE 1	6 months
ASC-H/HSIL cases after NC (n=27)					
Follow-up	CR cases	9	no recurrence		10-40 months
&	PR cases	12	NC add. 2	CONE 4	5-42 months
Add. Tx	NC cases	6	NC add.2	TVH 1, TLH 1 CONE 1	5-47months

## Follow-up after N<sub>2</sub>O cryotherapy (Table 3)

During 5 to 48 month follow-up, 14 CR ASC-US/LSIL cases and 9 CR ASC-H/HSIL cases showed no recurrence after N<sub>2</sub>OCryo. However, among 26 PR ASC-US/LSIL cases, 6 additional N<sub>2</sub>OCryo, 5 CONE, and 1 TLH required during follow-up. Among all 17 NC and PD cases, 6 additional N<sub>2</sub>OCryo, 3 CONE, 1 TVH and 1 TLH required during follow-up.

## Summary

**Colposcopy:** macroscopically lesions are disappeared after N<sub>2</sub>OCryo.

**Cytology:** microscopically LSIL are occasionally persistent after N<sub>2</sub>OCryo.

**HPVDNA level:** almost negative, but some are persistent after N<sub>2</sub>OCryo.

At present no recurrence are seen in CR cases, but further extensive follow-up would be necessary. However, even in short period, any better finding will be meaningful for CIN to avoid surgical treatment.

## Conclusion

Compared to LEEP or laser vaporization, N<sub>2</sub>O cryotherapy is an effective, safe, and acceptable treatment for CIN and it would be useful and mandatory with concurrent HPV test. Furthermore, it might be useful for HSIL cases to avoid CONE biopsy.

\* I declare I have no COI at this presentation.