High Resolution Microendoscopy (HRME): A Low-Cost Point-of-Care Diagnostic for Cervical Cancer Prevention

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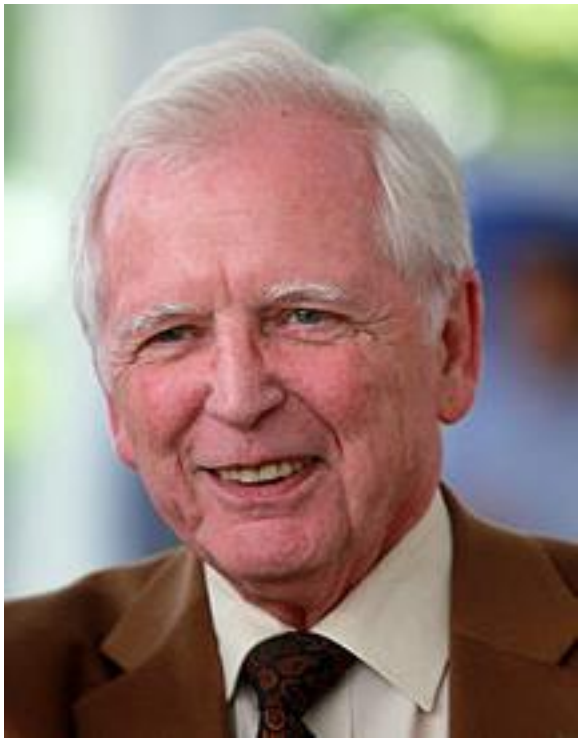
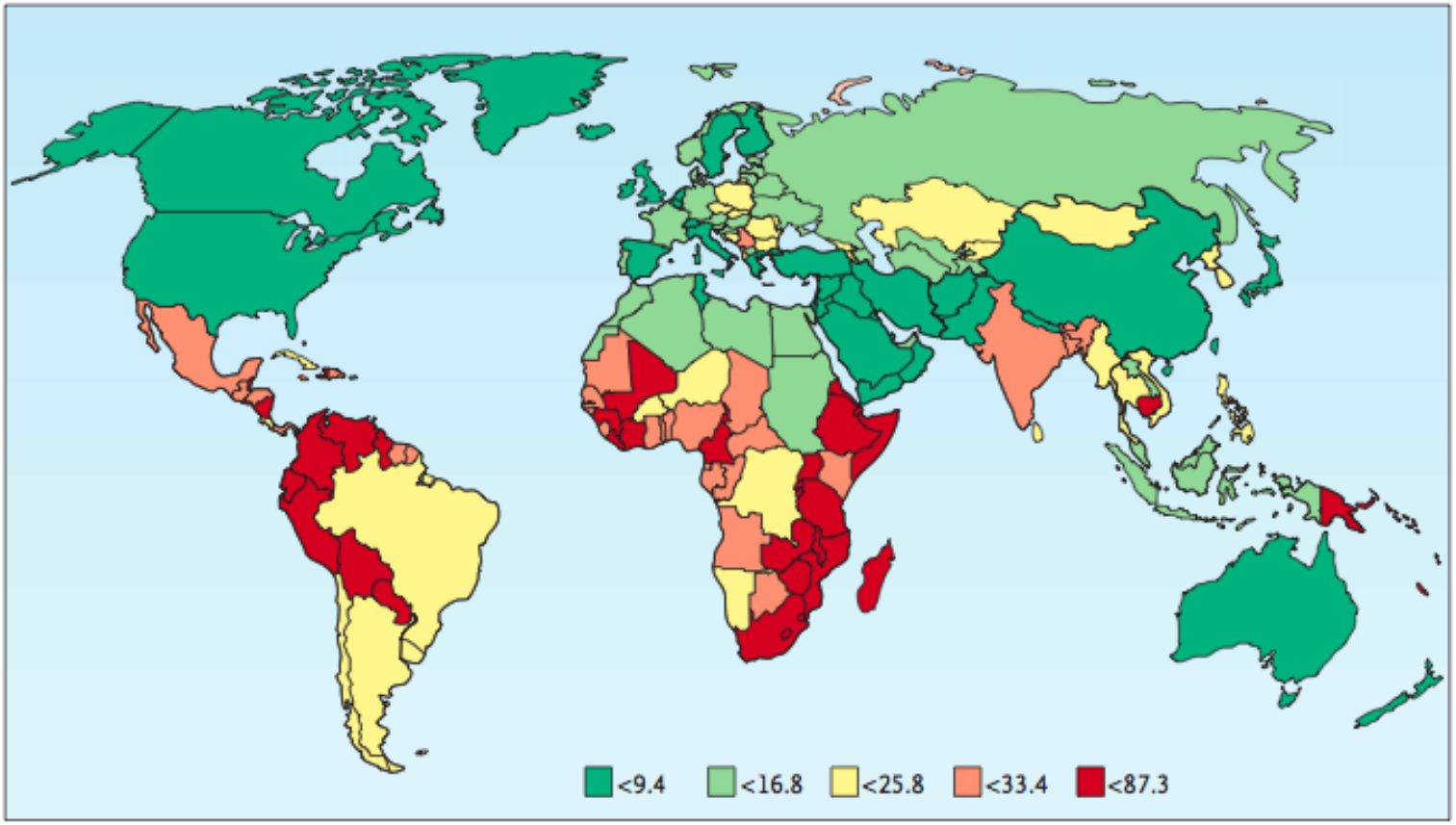
Cervical Cancer is Preventable

- **Known Etiology:**
  - **Human Papillomavirus (HPV)**
- **Prevention:**
  - **HPV Vaccination**
- **Screening:**
  - **Pap Test, HPV DNA Testing, VIA**
- **Treatable Pre-Invasive Phase:**
  - **Cervical Cone/LEEP/Cryotherapy**
  - **Takes ~10y to progress from pre-invasive disease to cancer**



Dr. Harald zur Hausen
Nobel Prize, 2008

Inequity of Cervical Cancer



Incidence of Cervical Cancer Worldwide.
Numbers indicate cases per 100,000 population.

85% of cervical cancer cases occur in the developing world

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Cervical Cancer Prevention in USA

Three Clinical Visits:

1. **Pap test +/- HPV testing**
2. **Colposcopy with cervical biopsies if abnormal Pap**
3. **If significant precancerous lesions (<5%) - conization/LEEP/cryotherapy**

   - Removal or ablation of precancerous lesion

**** Pathology/lab services required at each step**

**** Not feasible in low resource settings**

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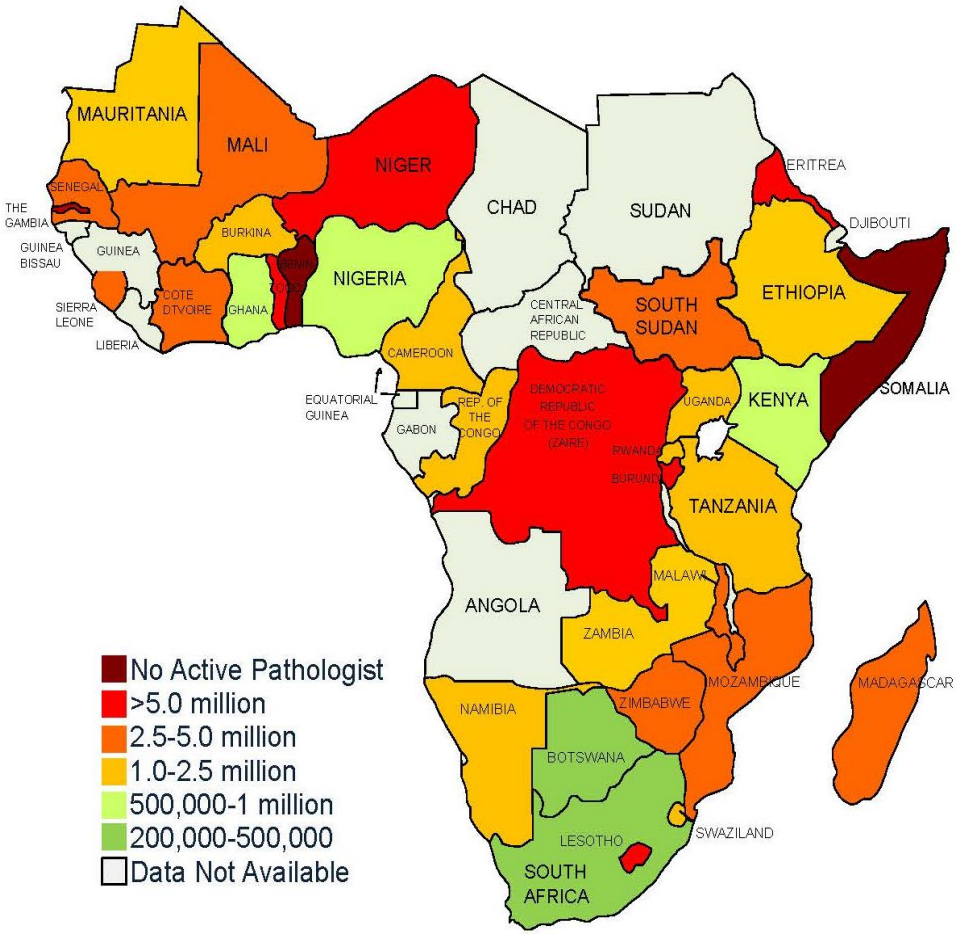
Availability of Pathologist



Number of People per Pathologist:

- UK: 15,108*
- US: 19,232**

*Royal College of Pathologists, 2012
**Anatomic and Clinical Pathologists, AAMC, 2007

Adesina et al., *Lancet Oncology*, 2012

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High-Resolution Microendoscope (HRME)

- **Novel cervical visualization technique**
- **Developed by Dr. Rebecca Richards-Kortum and team at Rice University**
- **Assesses morphologic features typically evaluated by pathologists in-vivo in real-time:**
  - **N/C ratio, nuclear size, atypia, pleomorphism**
- **Eliminates the need for colposcopy, cervical biopsies and pathology services**

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HRME

- **Proflavine (topical contrast agent that stains nuclei) is placed on cervix**
- **A fiber-optic probe is applied**
- **Fluorescence from the proflavine-stained epithelium is transmitted back to the HRME**
- **Image is displayed on a computer screen in <u>real-time</u> allowing for “See & Treat”**

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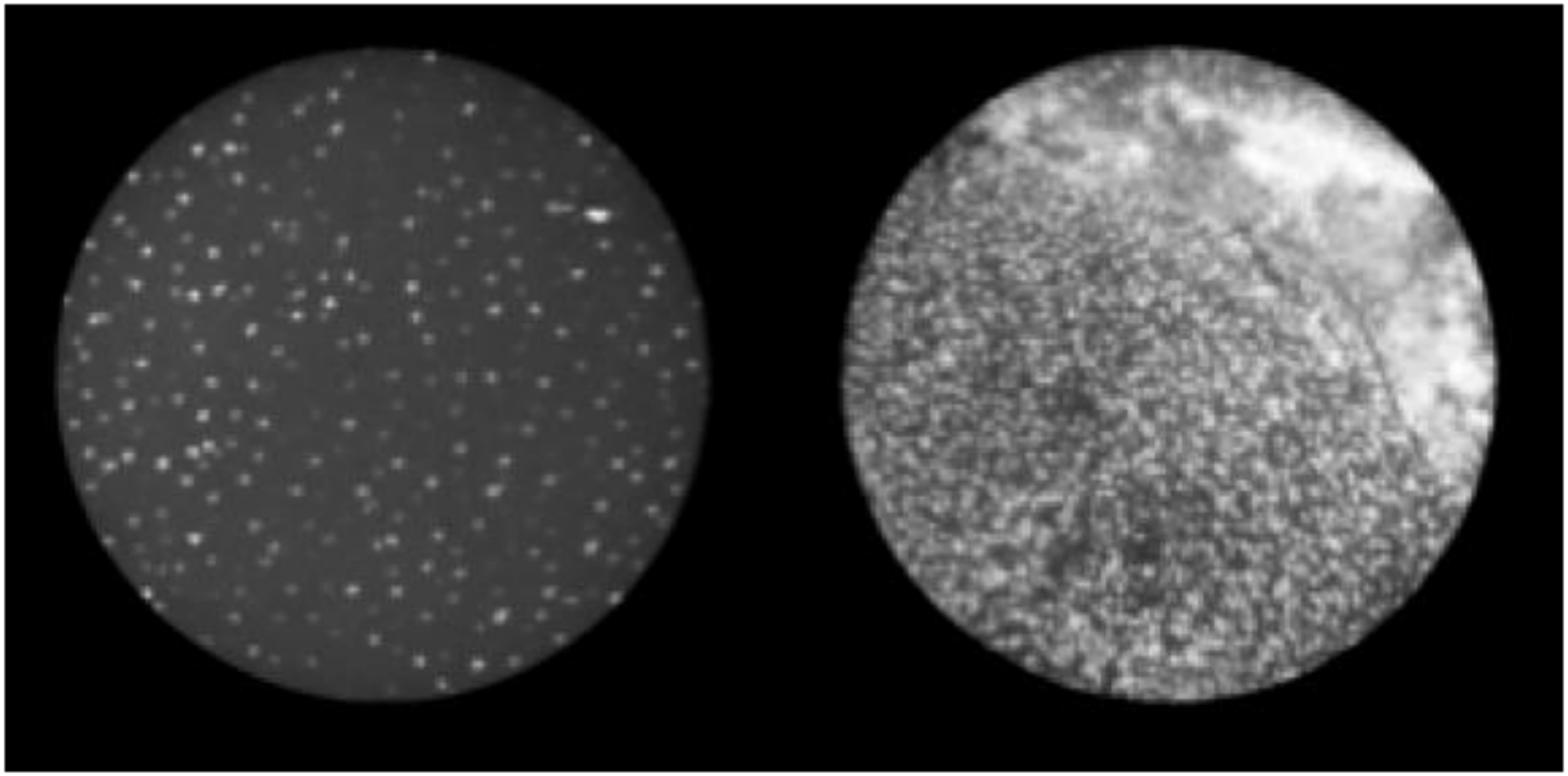
HRME - Normal vs. CIN2/3



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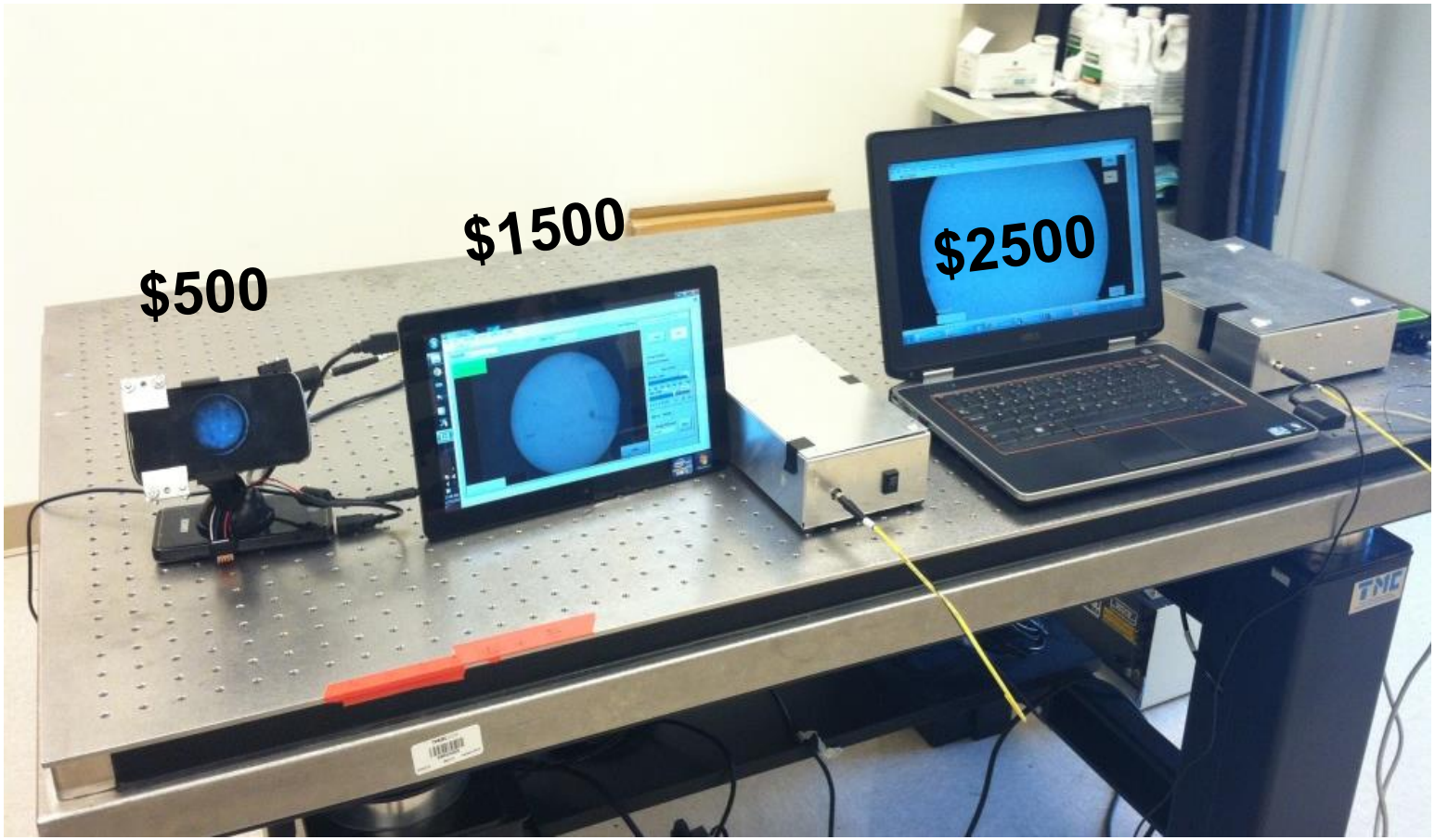
Reducing Size and Cost



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Pilot Study – Barretos, Brazil

- **Prospective study of 59 consecutive patients undergoing colposcopy for an abnormal Pap test**
- **HRME images obtained for all lesions noted on colposcopy and normal appearing areas**
- **Abnormal appearing areas were biopsied and reviewed by two independent, blinded pathologists as well as a US-based study pathologist**

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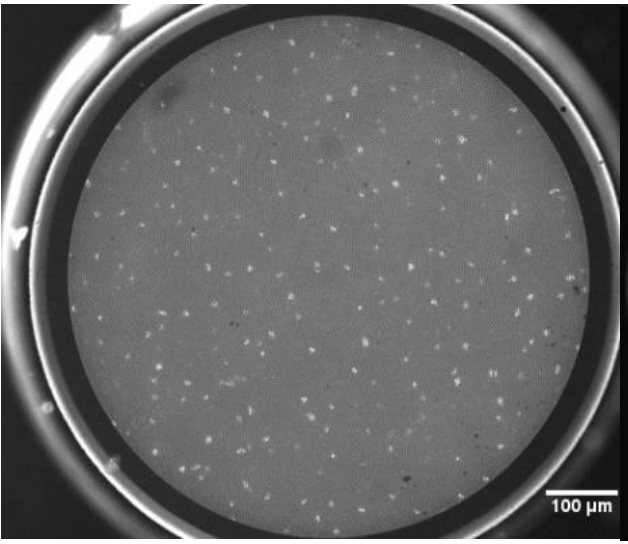
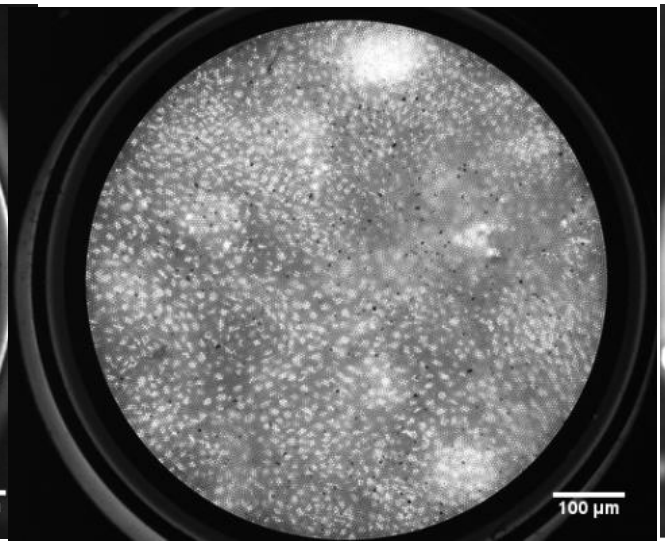
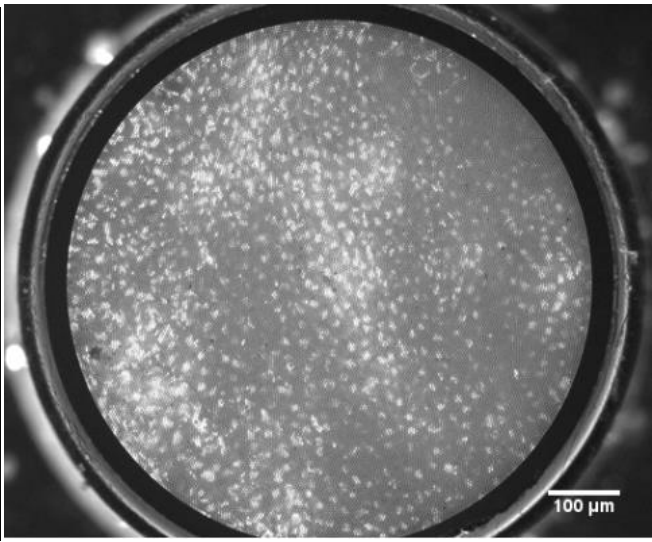
Barretos Cancer Hospital; 59 women referred for abnml Pap



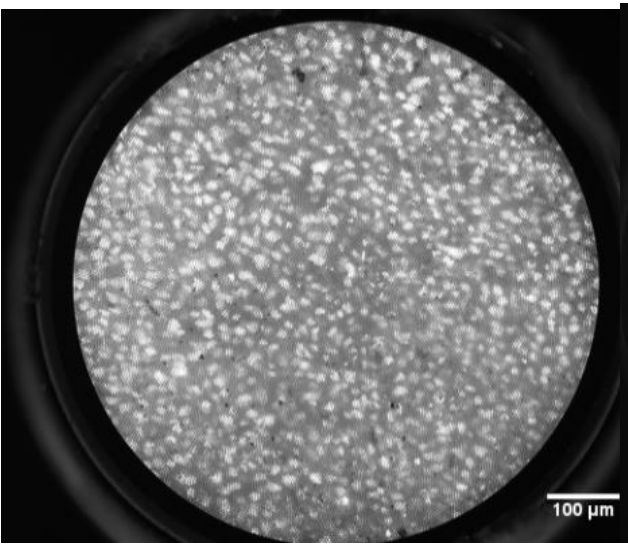
Normal



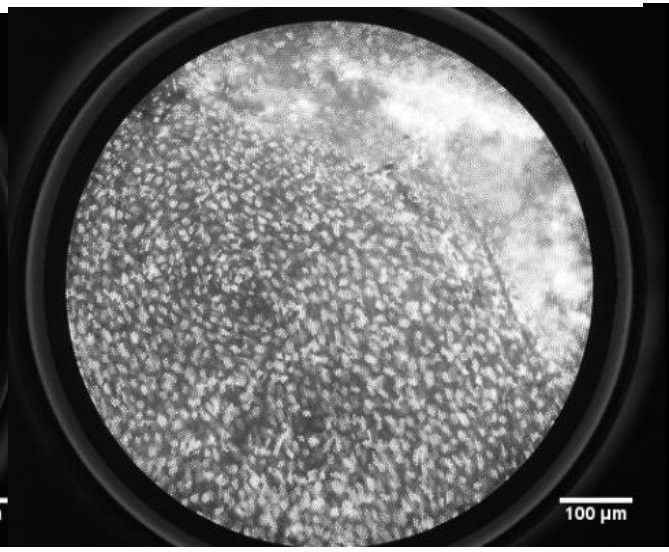
Inflammation



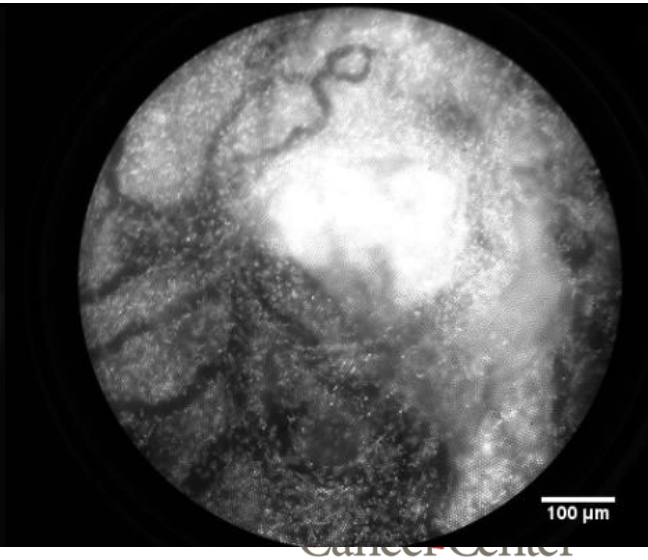
CIN 1



CIN 2



CIN 3



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Pilot Study – Barretos, Brazil

- **The N/C ratio, mean nuclear area and eccentricity were calculated from HRME images**
- **A diagnostic algorithm was developed to distinguish high-grade lesions (CIN2/3 and cancer) from less severe lesions (CIN1/benign)**
- **Performance was compared to histologic diagnosis**

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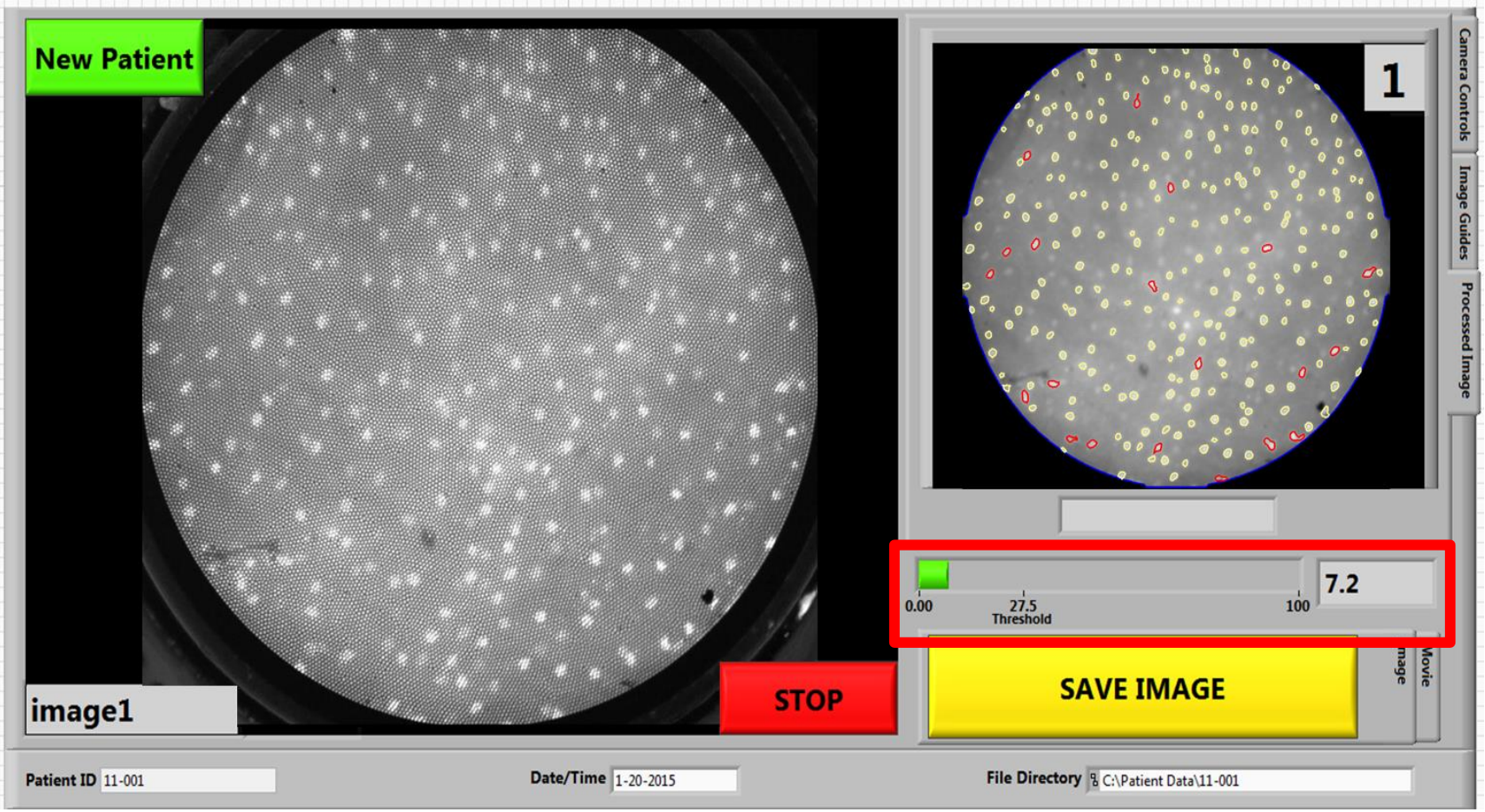
HRME - Objective Interpretation



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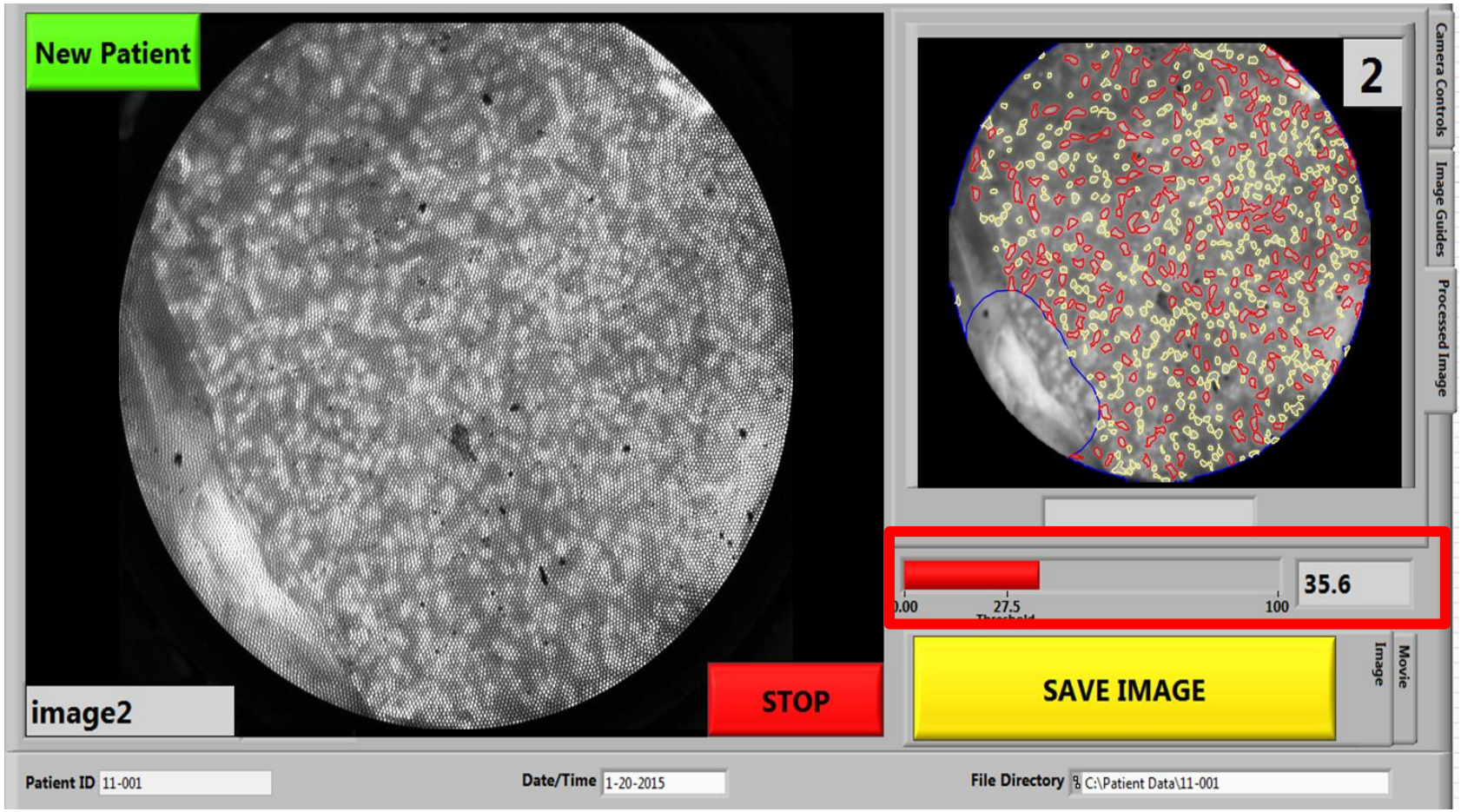
HRME - Objective Interpretation



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Pilot Study – Barretos, Brazil

- **A total of 79 acetowhite lesions were noted in 46 patients**
- **Biopsies were performed of all lesions**
- **Adequate HRME images were obtained in 59 of these lesions (75%)**

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Pilot Study – Barretos, Brazil

Diagnosis	Histology	HRME = CIN 2+
Normal	9 (15%)	22%
CIN 1	16 (27%)	31%
CIN 2	12 (20%)	83%
CIN 3	19 (32%)	95%
Cancer	3 (5%)	100%

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Conclusions

- **Pilot study demonstrated HRME accurately diagnose of CIN2+**
- **HRME imaging may provide a low-cost, accurate, point-of-care alternative to colposcopy and directed cervical biopsies**
- **Further evaluation in large prospective studies:**
  - **Houston, Texas-Mexico border, El Salvador, mobile units in rural Brazil**

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UH2 – Low Cost Technology Program

- **Incorporate HRME in a mobile diagnostic and treatment unit**
- **Pilot study of 200 women**
- **Compare rates of treatment completion for screen+ women (mobile unit in their local area vs. traveling to a central facility)**

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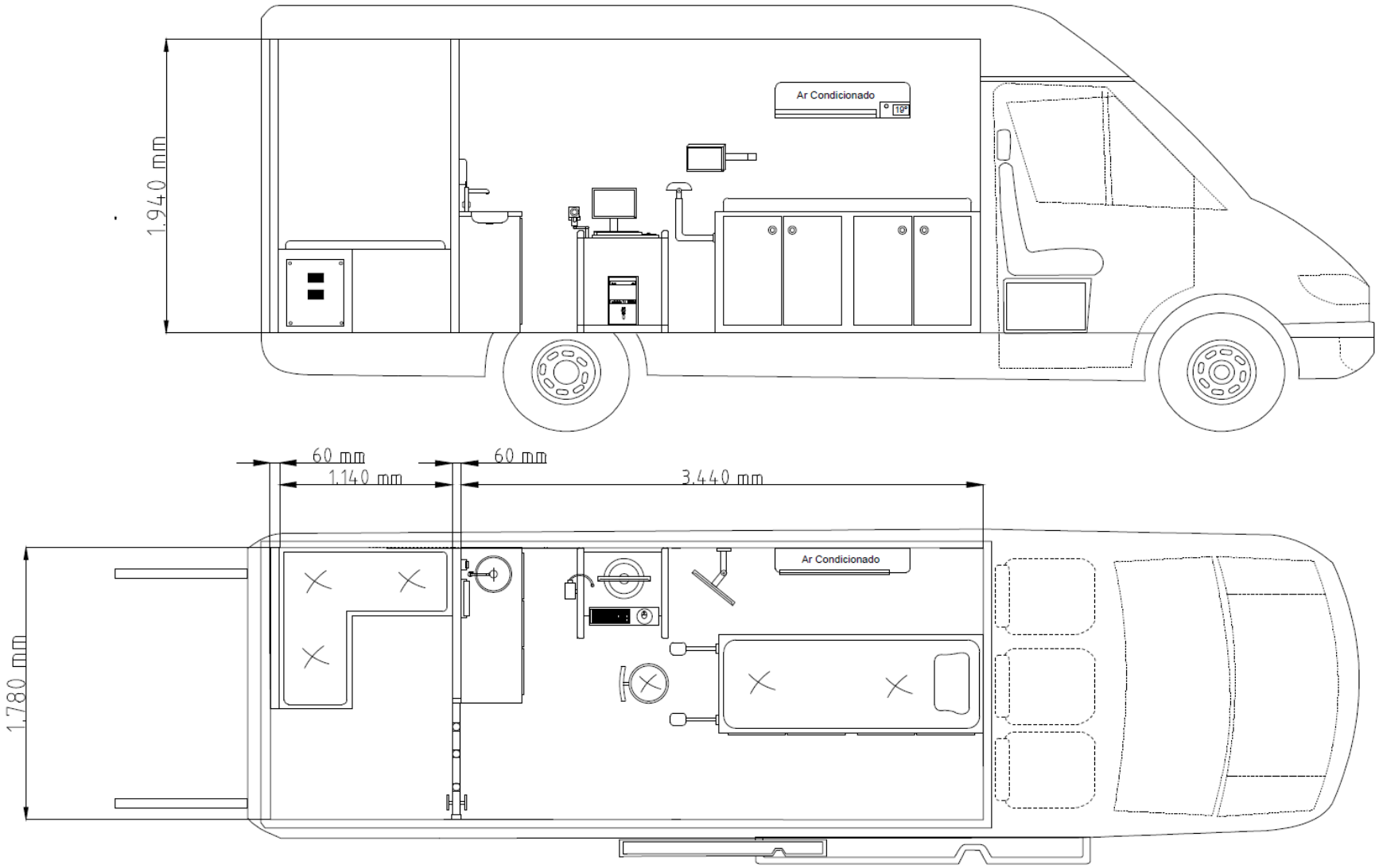
Colposcopy/HRME/Cryo Unit



Acknowledgements

- José Humberto Fregnani
- Rebecca Richards-Kortum
- Benjamin Grant
- Tim Quang
- Julio Possati Resende
- Cristovam Scapulatempo
- Graziela Macedo
- Edmundo Mauad
- Philip Castle
- Mark Stoler
- Cindy Melendez
- Juana Rayo
- Jessica Gallegos
- Jessica Limbrick
- Talita Garcia do Nascimento
- Naitielle de Paula

Funded by the MD Anderson Sister Institution Network Fund & NCI Center for Global Health (HHSN261200800001E and UH2)

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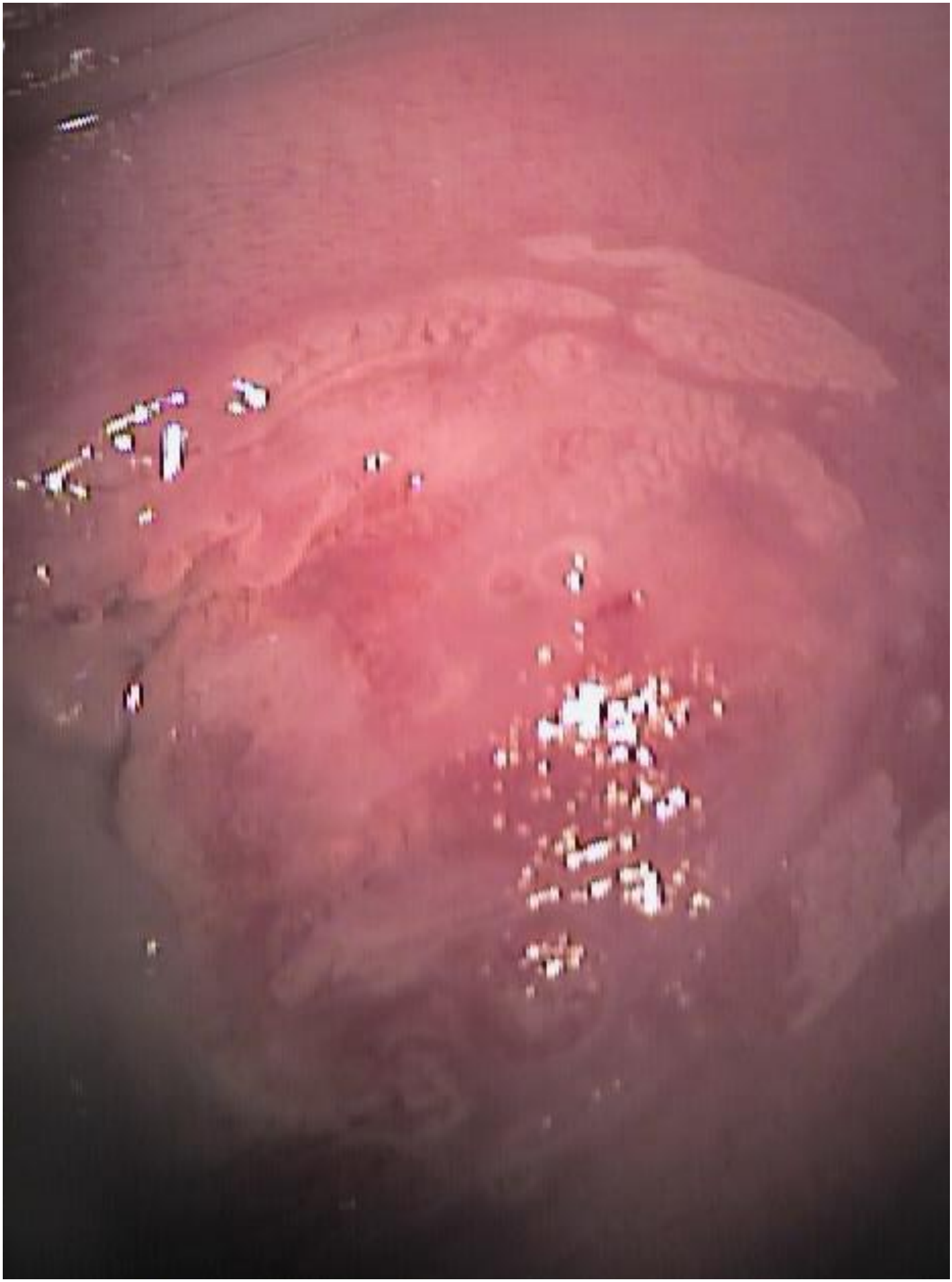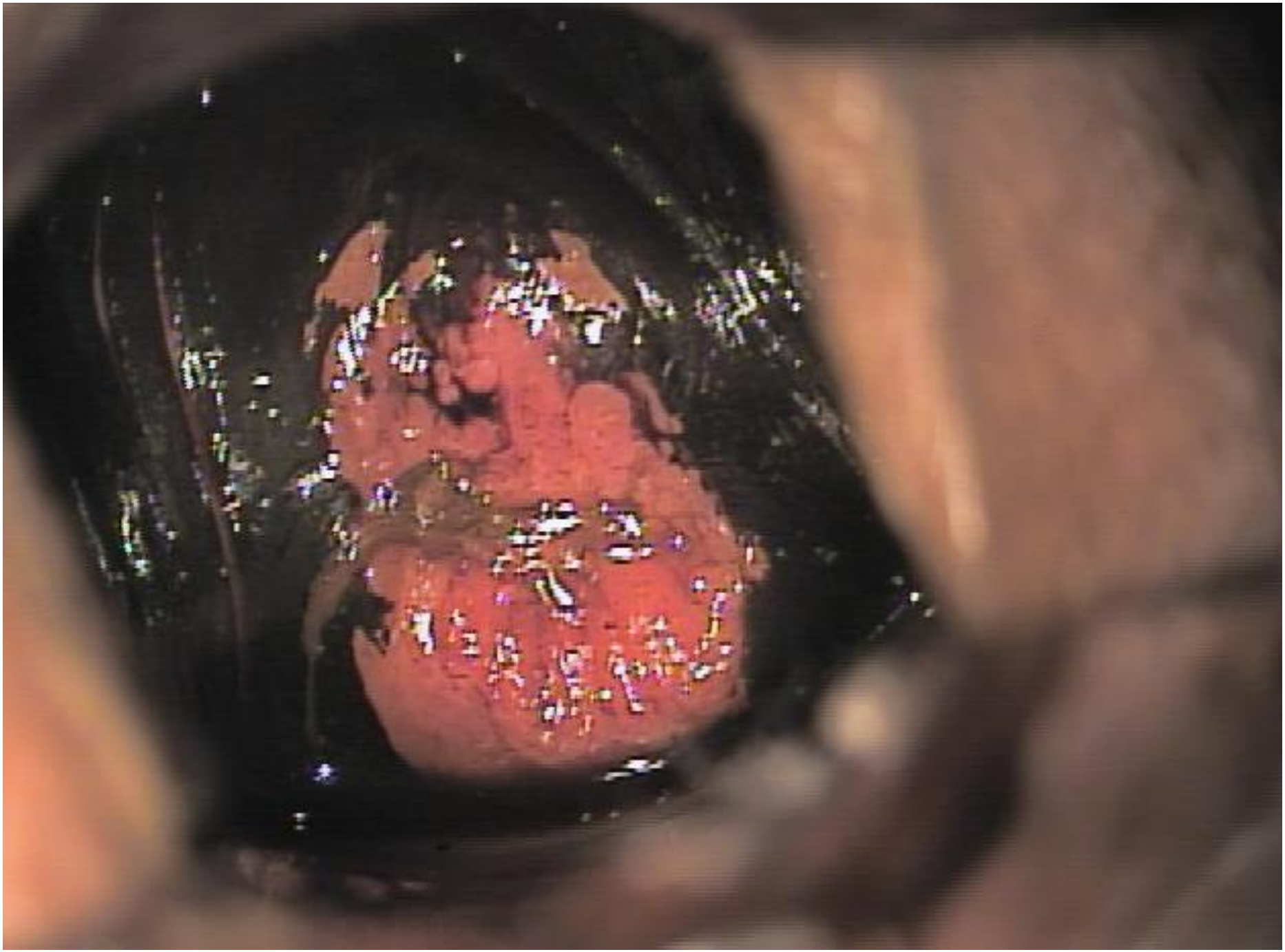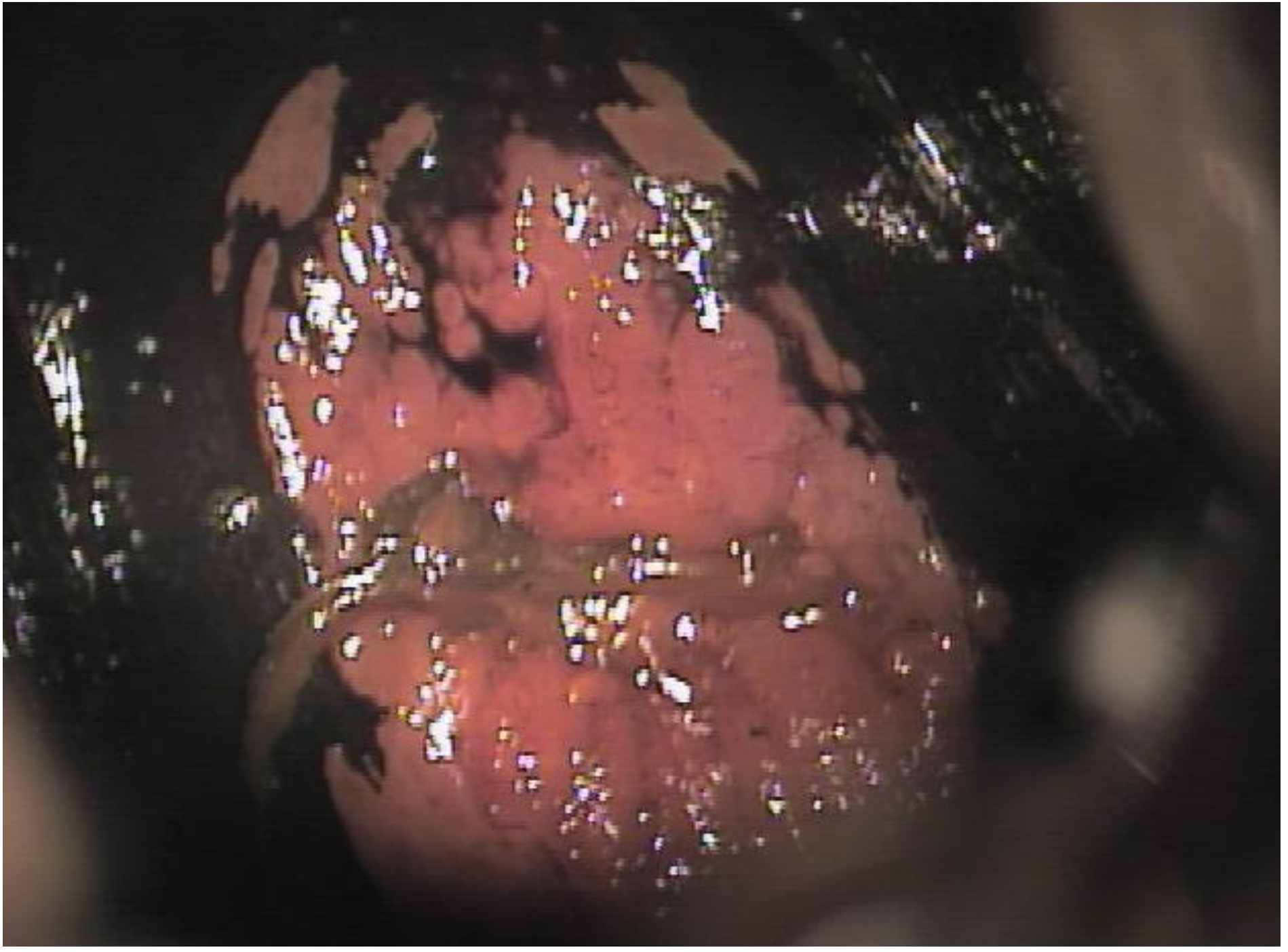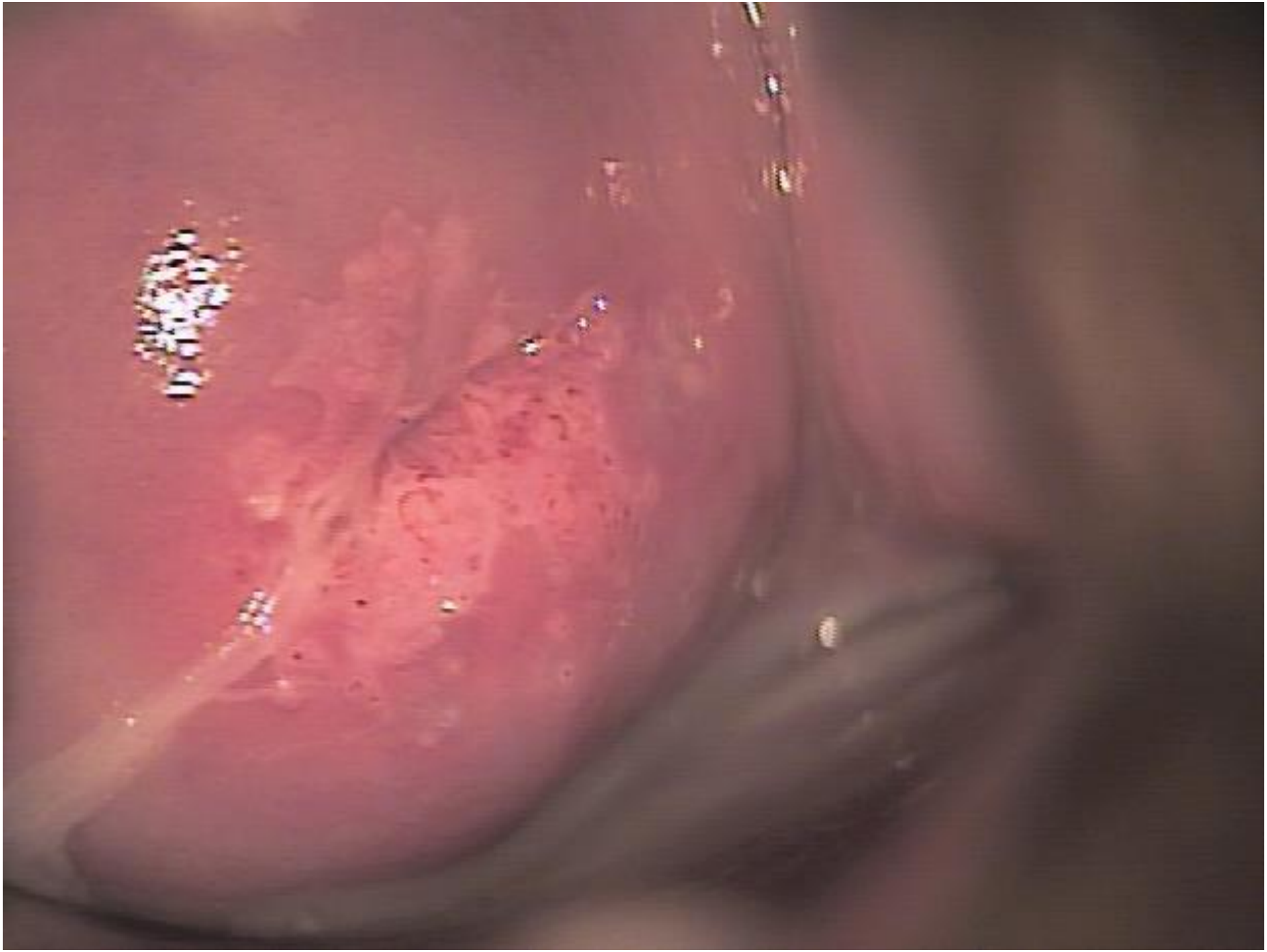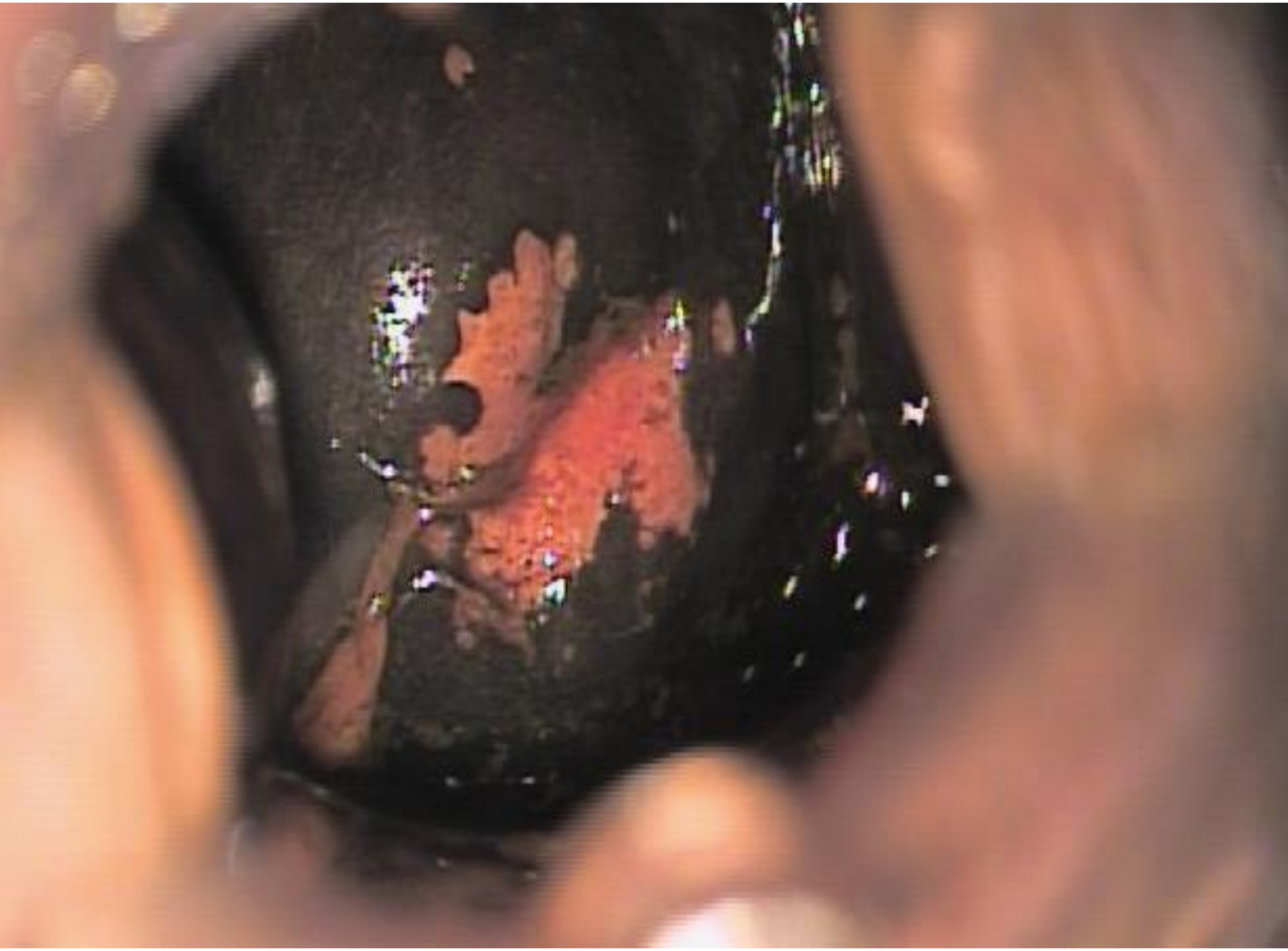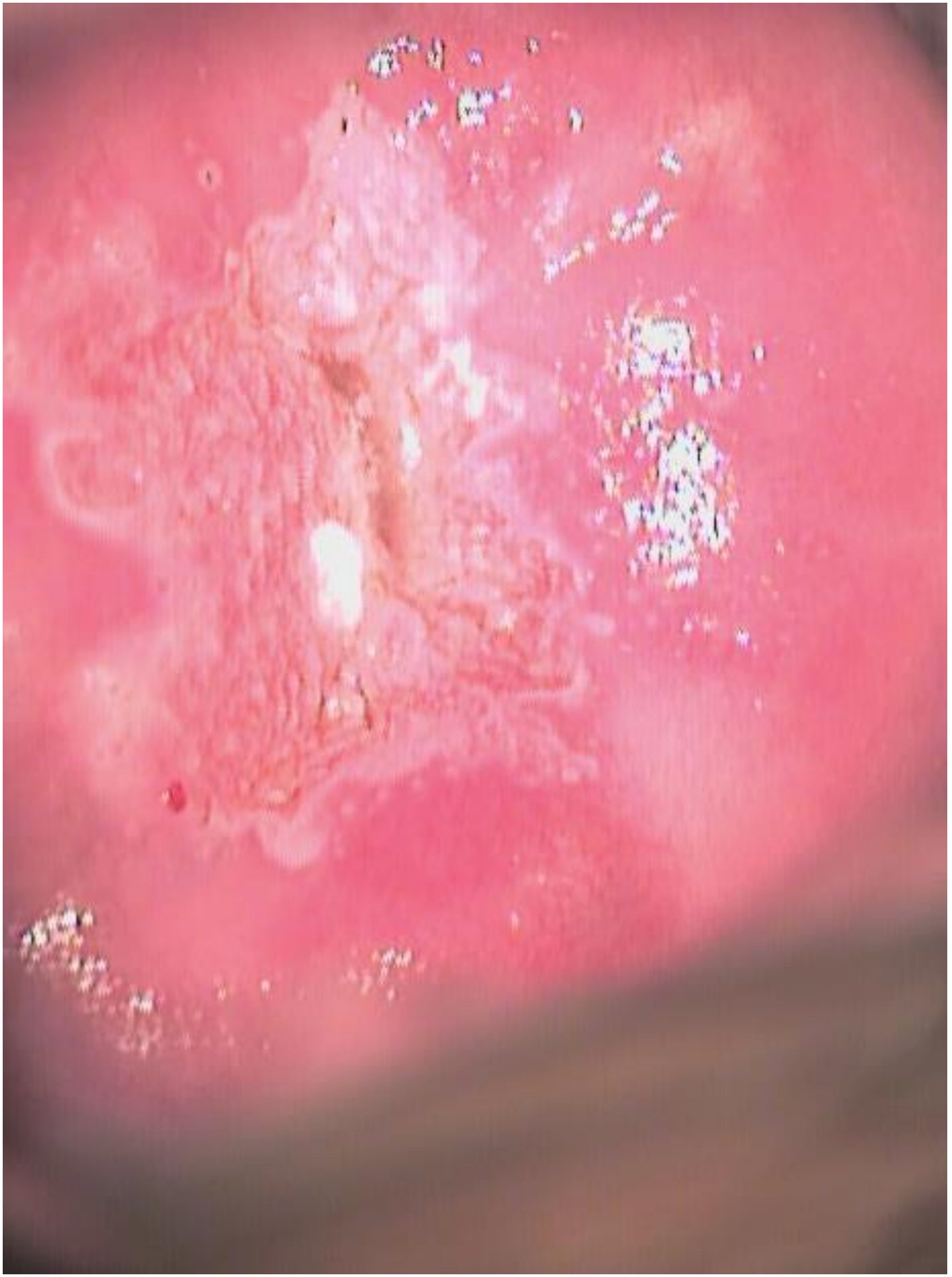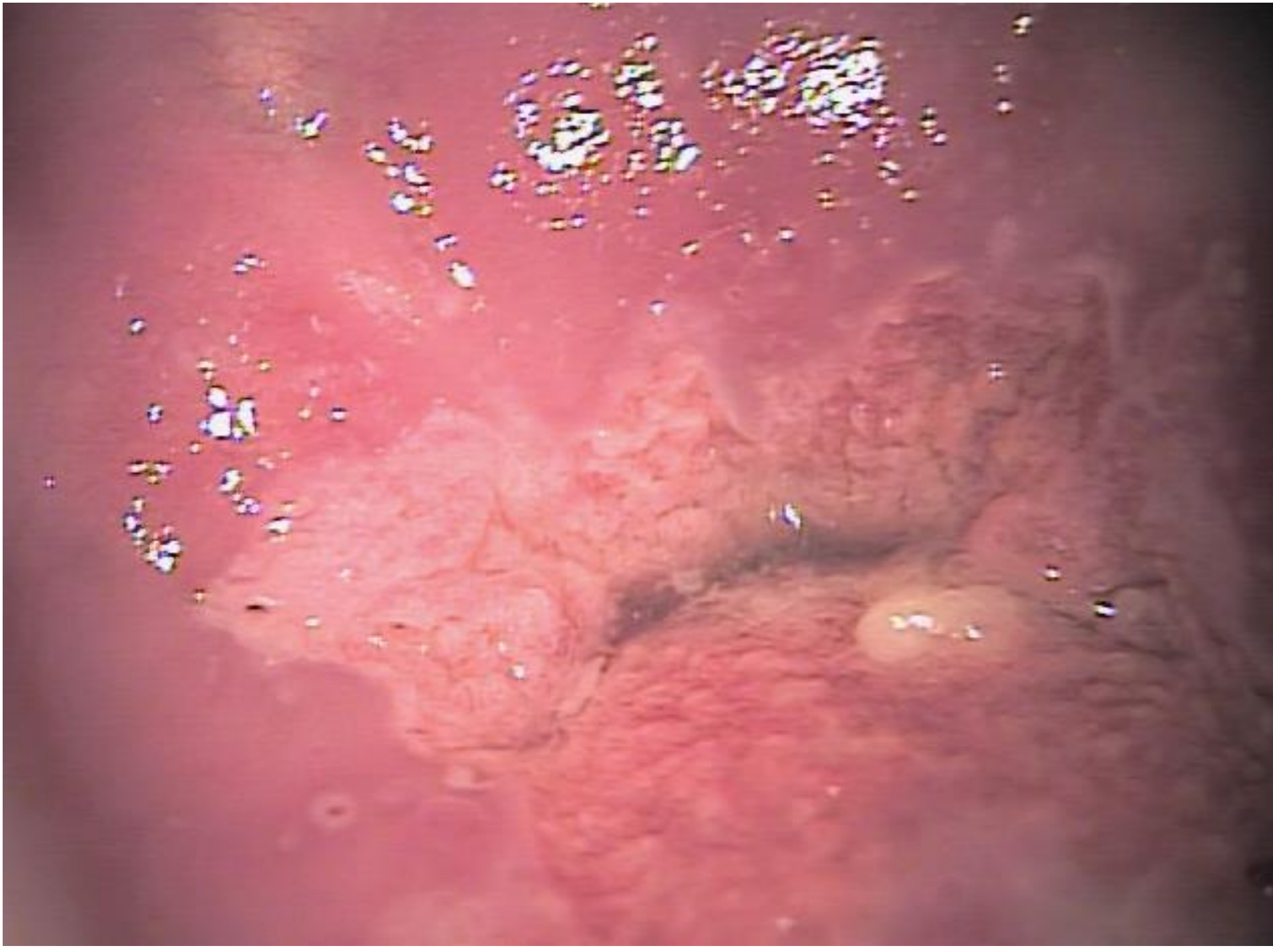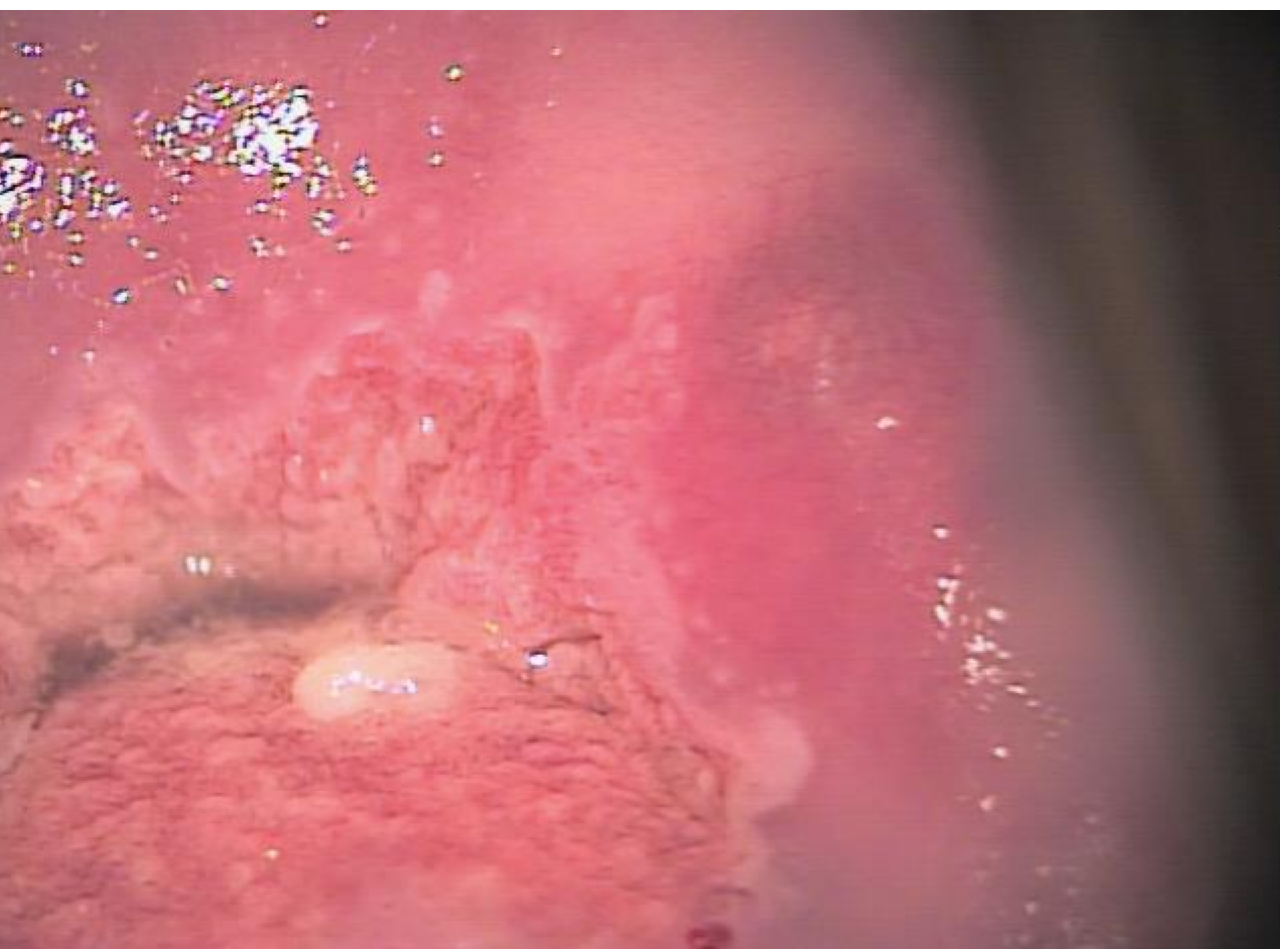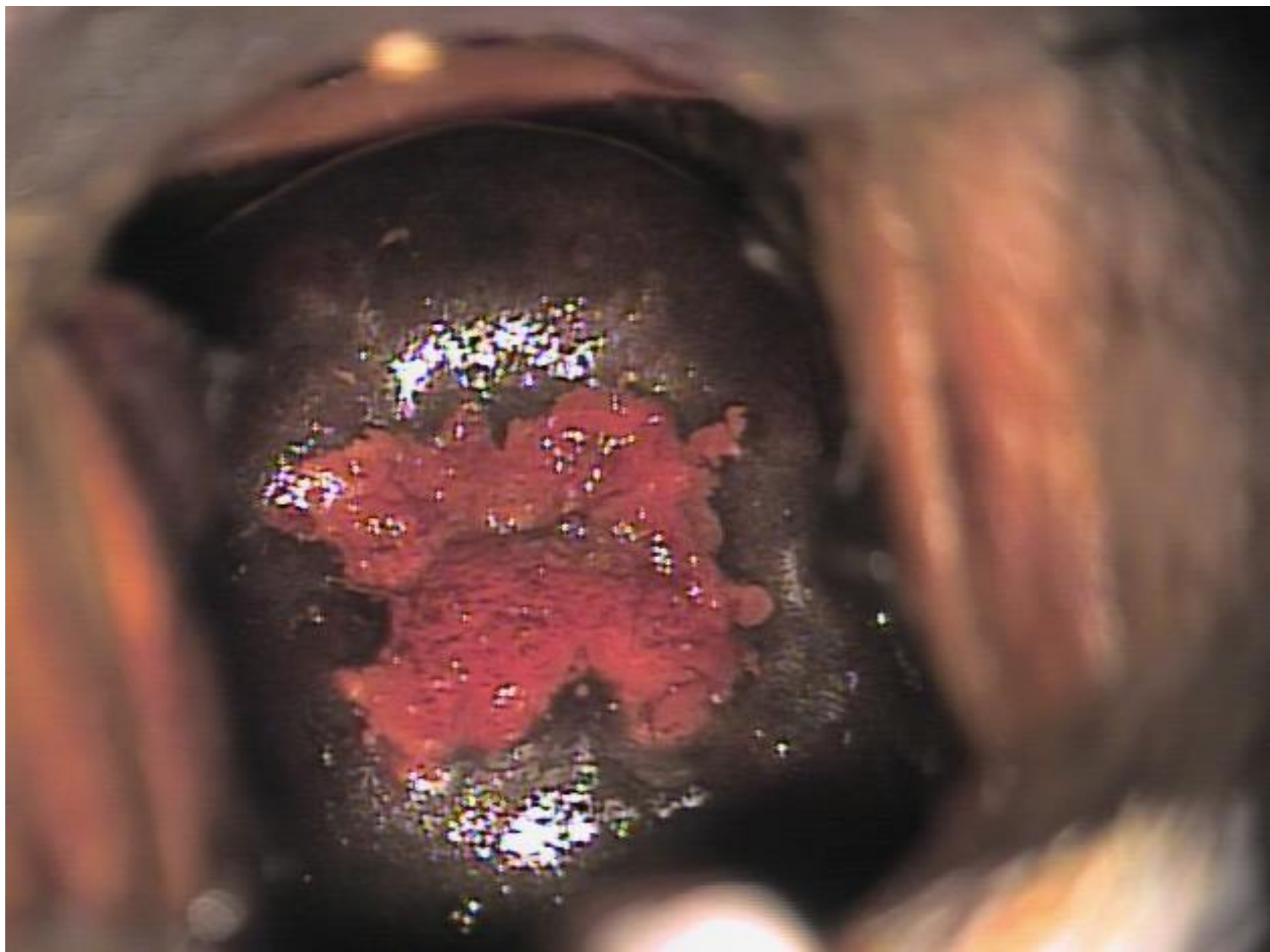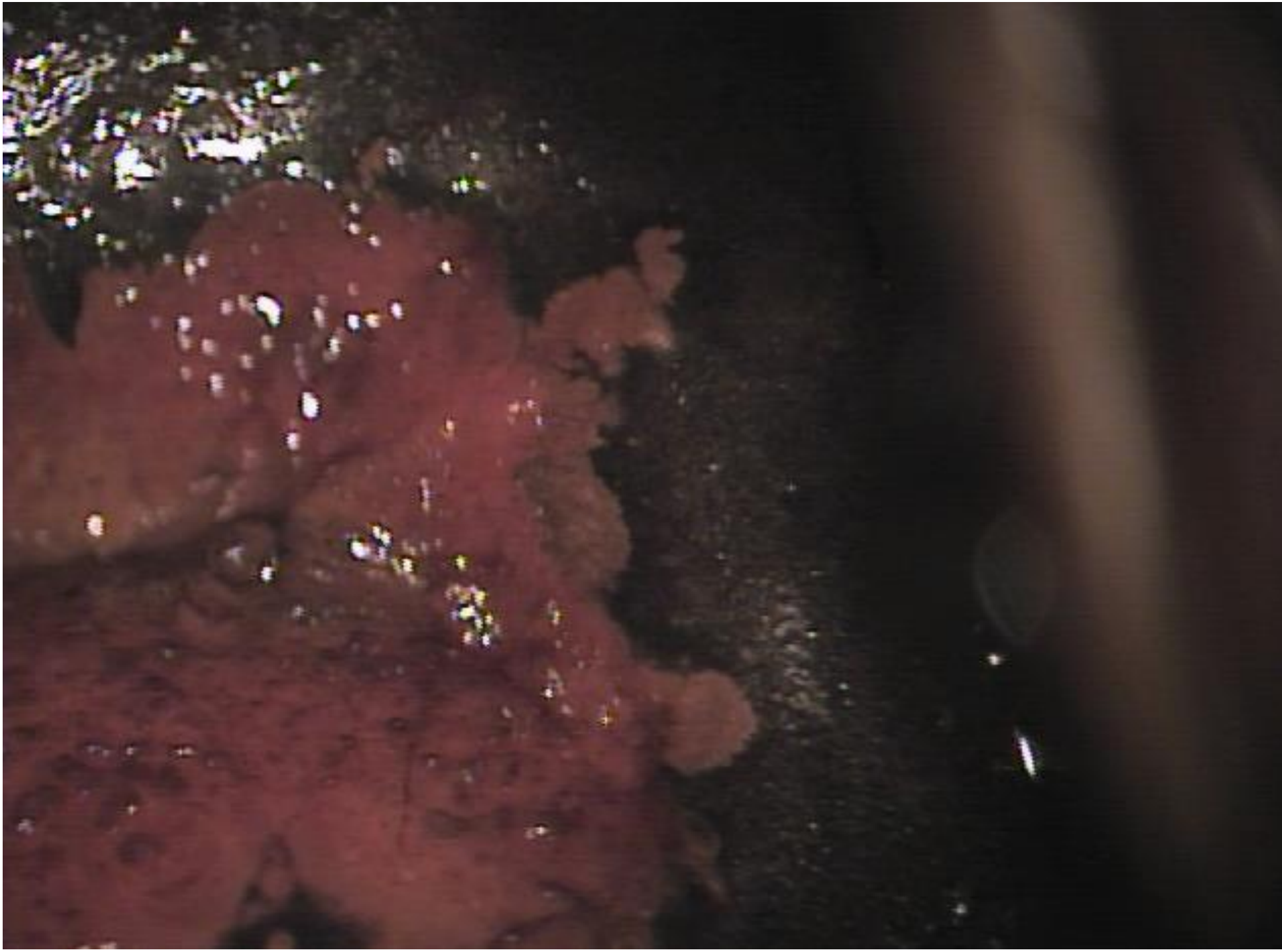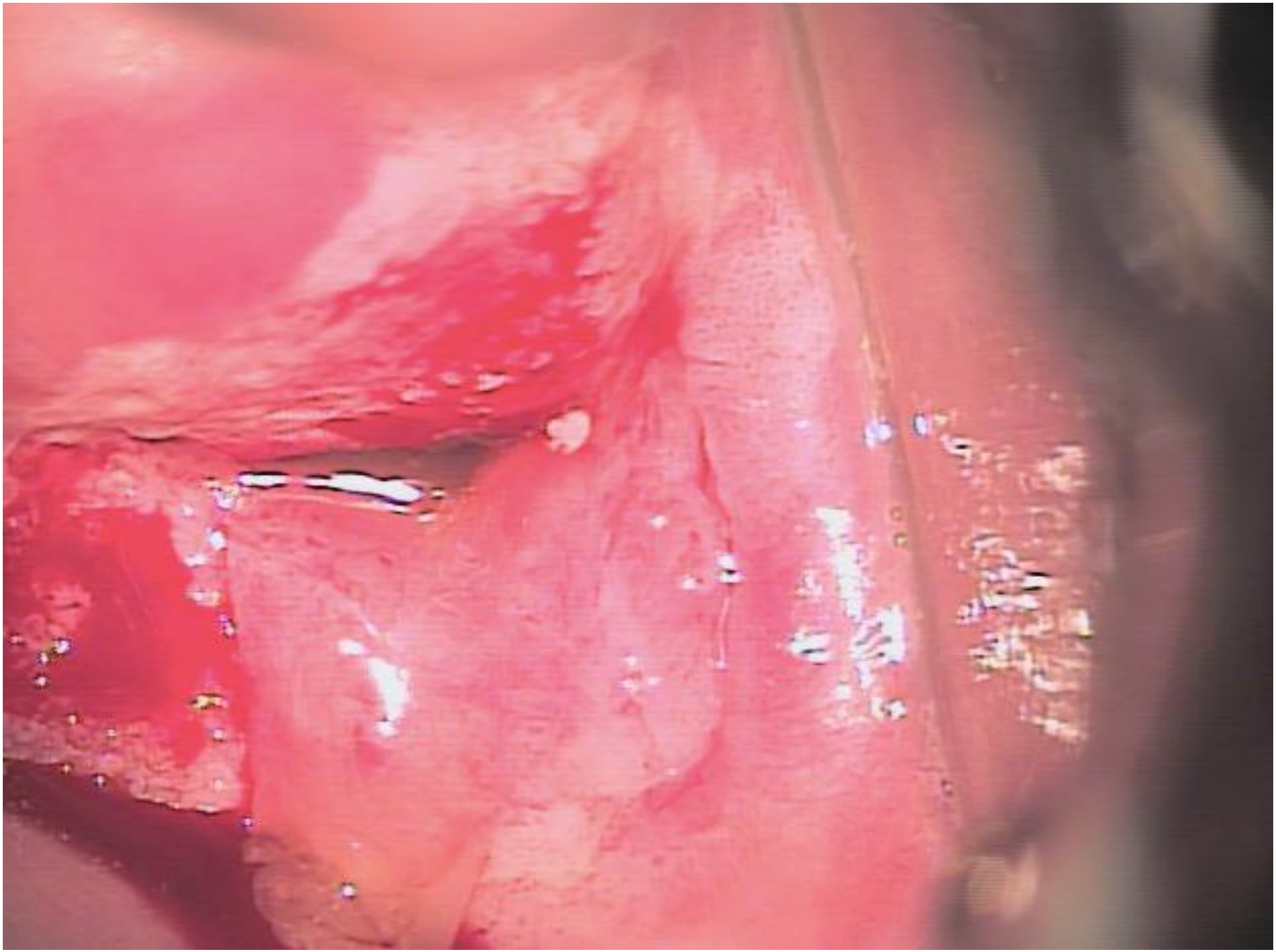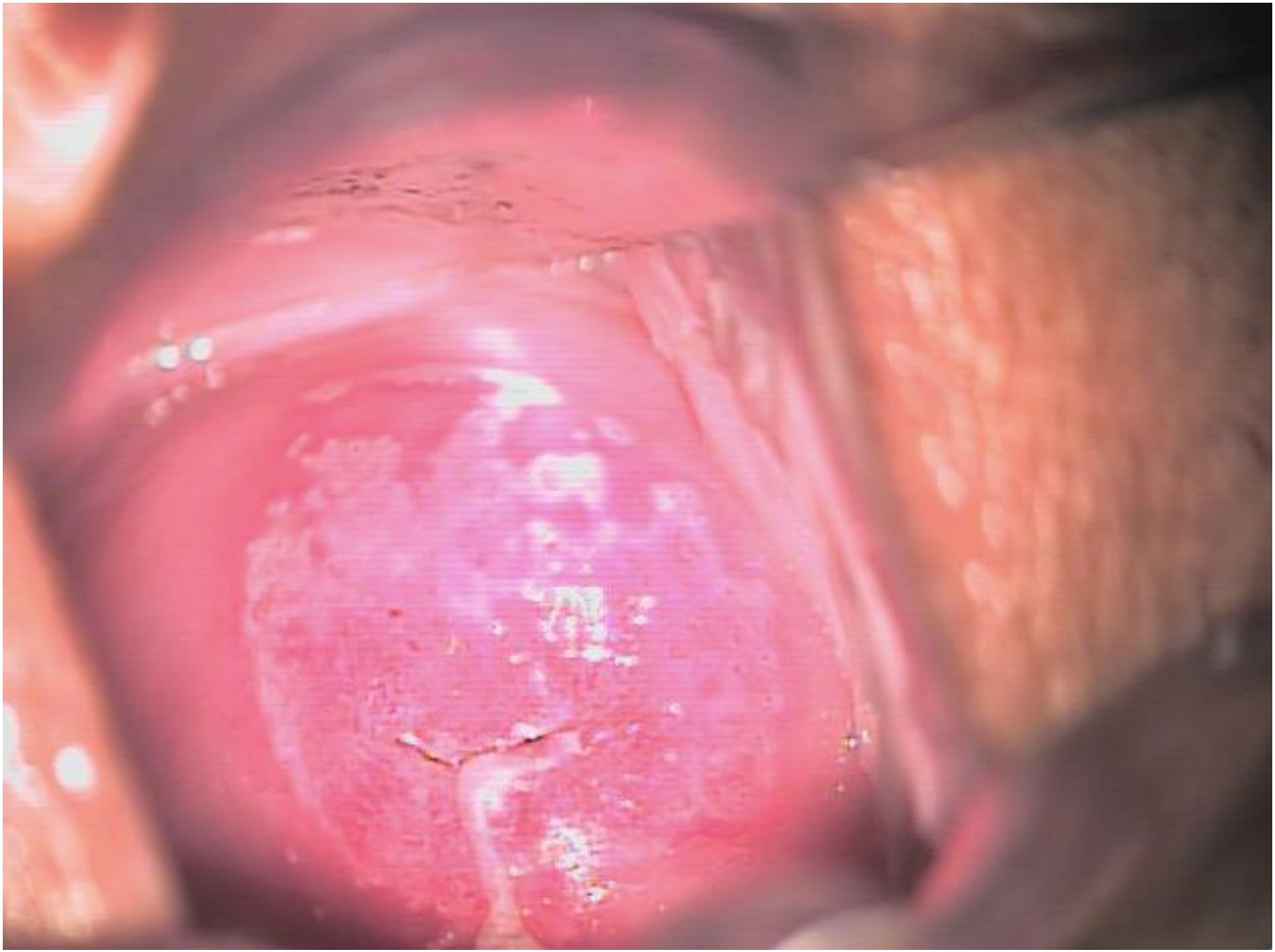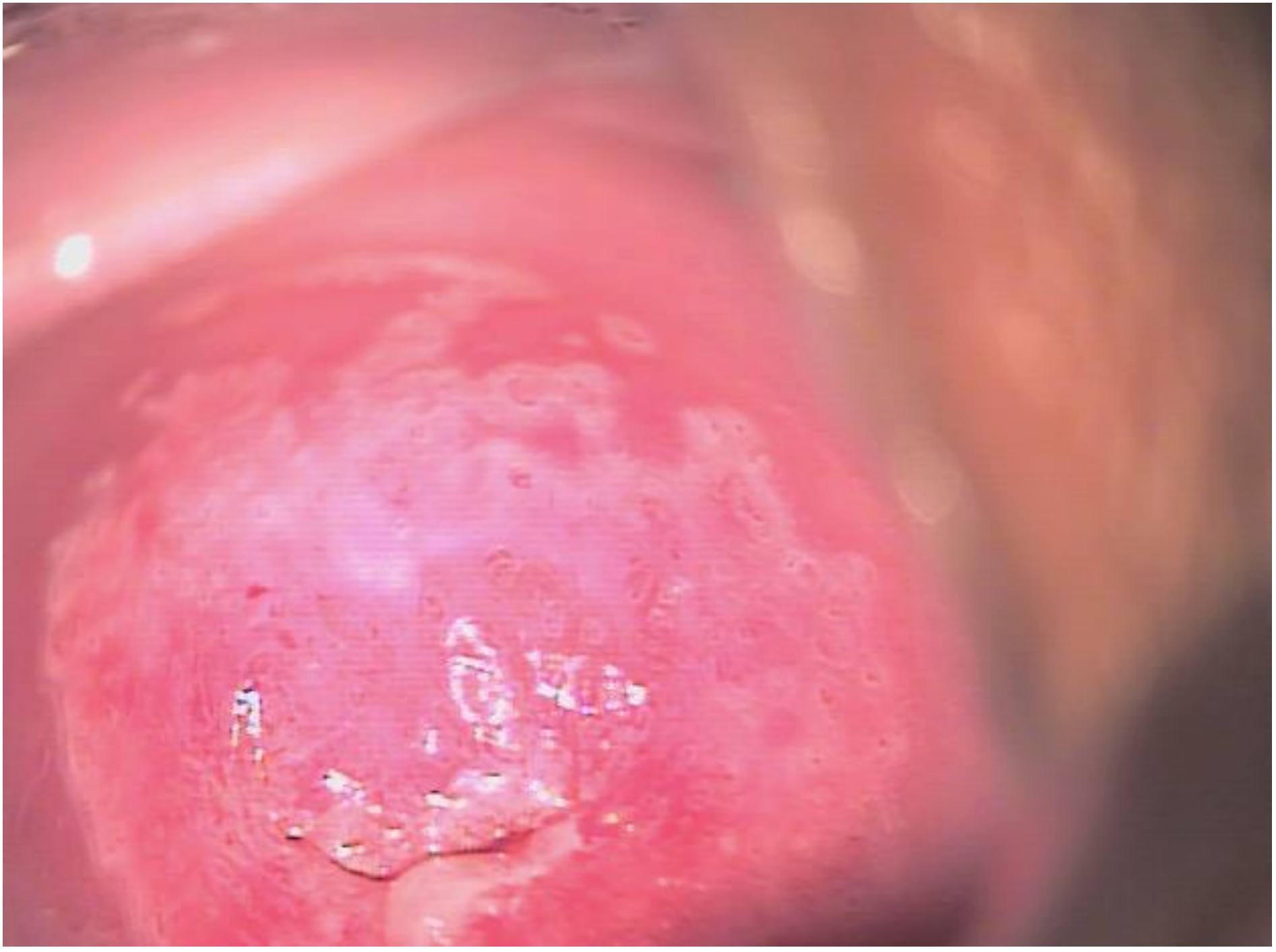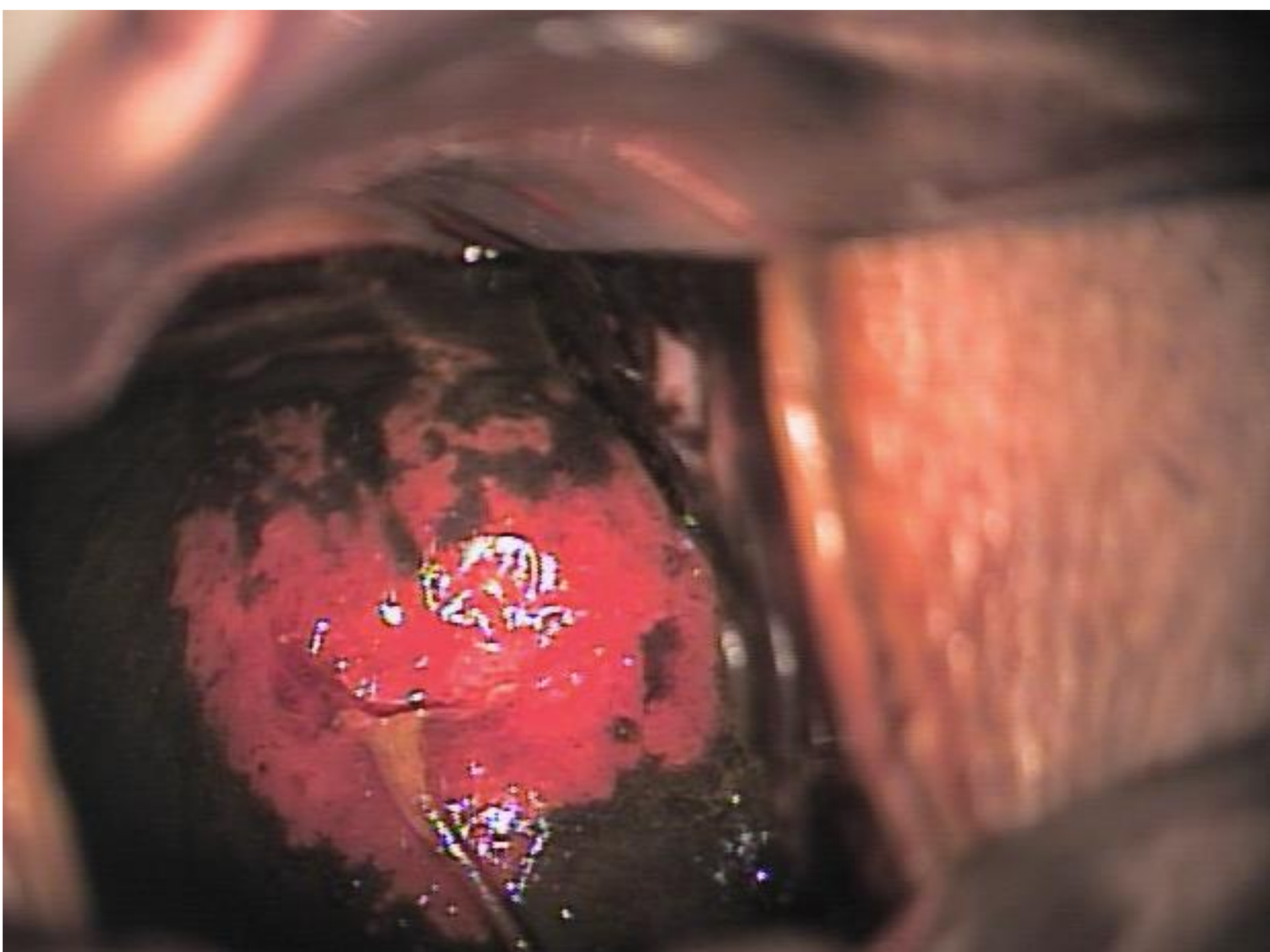
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