Hypothesis / aims of study
Cystoscopic evaluation has been recommended as a routine examination for the diagnosis of IC/BPS according to the EAU guideline whereas IC/BPS is diagnosed based on the patients’ symptoms, and cystoscopic evaluation is not mandatory in the current AUA guideline. However, phenotyping of the disease to identify the bladder specific pathology would be important for tailored treatments of IC/BPS. For instance, when Hunner lesions are identified by cystoscopy, laser or fulguration of the lesion can be helpful in the management of pain and frequency of IC/BPS. However, atypical Hunner lesions are often missed, and glomerulations, which are the diagnostic criteria of non-Hunner type IC and defined as multiple petechia-like hemorrhages shown after bladder hydrodistension, are reportedly not the specific observation of IC/BPS [1]. A previous study has shown that the narrow-band imaging (NBI) system, which can evaluate structures of capillaries within the superficial mucosa of hollow organs including the bladder, is useful to identify Hunner lesions, which would have been missed using a conventional white light cystoscope [2]. In this study, we extended our previous study to investigate whether the NBI system is useful to identify and characterize mucosal lesions under local anaesthesia without bladder distension, which are a predisposition to glomerulations or petechial bleeding seen after bladder hydrodistension, for the diagnosis of non-Hunner IC/BPS.

Study design, materials and methods
Under local anaesthesia with 20 ml of 4% lidocaine instilled into the bladder, we evaluated the bladder mucosa using a flexible cystoscope with NBI in 430 cases diagnosed for IC/BPS based on their symptoms. Using a NBI cystoscope with illumination at two wavelengths of 415 nm and 540 nm, capillary blood vessels in the superficial bladder mucosa and large blood vessels in the deeper mucosal layer are silhouetted in brown and blue colour, respectively, to enhance the contrast of superficial vascularity in the bladder mucosa. After baseline evaluation of the entire bladder mucosa, patients were divided to those with classical IC with Hunner lesions or with non-Hunner type IC/BPS.

Results
Among 430 cases, 415 patients (96.5%) showed the hypervascular, overstretched bladder mucosa before bladder distension whereas the remaining 15 cases exhibited the folded whitish mucosa with few vessels, similar to the appearance of normal bladder (Fig. 1). In these 415 cases with hypervascular, stretched mucosa, NBI-assisted cystoscopy revealed Hunner lesions in 191 cases (46.0%) (Fig. 2) and non-Hunner lesions that are characterized by spotty, superficial neovascular lesions identified without bladder distension, which showed glomerulations or petechial bleeding when the bladder was overdistended (Fig. 3), in 222 cases (53.5%). In addition, non-Hunner lesions were also observed in all cases with Hunner lesions, indicating that Hunner and non-Hunner lesions coexist in IC/BPS bladders. The remaining 2 cases (0.5%) exhibited cystitis cystica-like diffused cystic lesions.

Interpretation of results
1. IC/BPS bladders exhibit the stretched mucosa with increased vascularity under the non-distended condition (Fig. 1).
2. NBI-assisted cystoscopy increases the accuracy of identification of Hunner lesions (Fig. 2).
3. IC bladders with Hunner lesions also had non-Hunner lesions detected by NBI-cystoscopy.
4. NBI-assisted cystoscopy under local anaesthesia enables to identify non-Hunner lesions of IC/BPS bladders, which are characterized by spotty, superficial neovascular lesions on the mucosal surface without bladder distension, which would have been missed by a conventional white light cystoscopy (Fig. 3).

Concluding message
By using the NBI system we detected not only Hunner lesions, but also non-Hunner lesions that are characterized by spotty, neovascular mucosal lesions without bladder distension in the majority of IC/BPS patients who were diagnosed based on their symptoms (413 [191 Hunner+222 non-Hunner] out of 430 patients; 96%). The hypervascular, overstretched condition of the bladder mucosa and non-Hunner lesions with or without Hunner lesions found in the majority of IC/BPS patients may indicate that these patients have a hypersensitive condition of the bladder underlying IC/BPS symptoms. Thus, NBI-assisted cystoscopy under local anaesthesia would be useful to identify the bladder-specific pathology for the tailored treatments such as bladder-targeting intravesical therapy for cases with non-Hunner lesions only or Hunner lesion-targeting fulguration therapy in IC/BPS.
Fig. 1: Normal vs. Hypervascular, overstretched IC bladder mucosa

Fig. 2: Hunner lesions (white light vs. NBI)

Hunner lesions (arrows) seen as “reddened mucosal areas” under conventional white-light cystoscopy (left) are more easily recognized with the NBI system (right).

Fig. 3: Non-Hunner lesions

In cases without Hunner lesions, spotty, neovascular mucosal lesions (arrows in middle panel) are recognized as non-Hunner lesions with the NBI system, which were not clearly seen under conventional white-light cystoscopy (left panel). When the bladder is distended, these mucosal regions often show the glomerulations (arrows in right panel) with petechial bleeding.

References

Disclosures
Funding: None Clinical Trial: No Subjects: HUMAN Ethics not Req’d: it was based on the routine cystoscopic evaluation under government approval. Also, all patient data were de-identified before analysis. Helsinki: Yes Informed Consent: Yes