

Urinary Tract Infections and Encrustation in Urinary Stents



Roman Herout, Alina Reicherz, Ben H. Chew, and Dirk Lange

1 Introduction

Ureteral stents are hollow tubes that ensure urine flow from the kidney via the ureter into the bladder. First introduced by Zimskind in 1967, the modern “double pigtail” or “double J” ureteral stent, as we know it today, was developed by Finney et al. in 1978 [1, 2]. Since then, ureteral stents have been broadly used in the field of Urology for various indications such as blocking ureteral calculi, following endoscopic procedures, as well as reconstructive procedures such as uretero-ureterotomy or pyeloplasty. In addition, long-term stenting is frequently required in patients with malignancies to relieve obstruction of a compressed ureter. Besides warranting antegrade urine flow, these stents can also protect an anastomosis and serve as a scaffold in the healing process.

R. Herout

Department of Urologic Sciences, The Stone Centre at Vancouver General Hospital,
University of British Columbia, Vancouver, BC, Canada

Department of Urology, University Hospital Carl Gustav Carus, Technische Universität
Dresden, Dresden, Germany

e-mail: roman.herout@ukdd.de

A. Reicherz

Department of Urologic Sciences, The Stone Centre at Vancouver General Hospital,
University of British Columbia, Vancouver, BC, Canada

Department of Urology, Ruhr-University of Bochum, Marien Hospital Herne,
Herne, Germany

e-mail: alina.reicherz@rub.de

B. H. Chew · D. Lange (✉)

Department of Urologic Sciences, The Stone Centre at Vancouver General Hospital,
University of British Columbia, Vancouver, BC, Canada

e-mail: ben.chew@ubc.ca; dirk.lange@ubc.ca

Regardless of their clinical benefits, these indispensable tools for everyday practice come with substantial hindrances as they can lead to stent-related symptoms, encrustation, hematuria, infection and hence to an overall reduction in the quality of life of patients [3].

2 The Complex Interaction Between Bacteria, Biofilm and Urinary Tract Infections

Bacterial colonization of foreign bodies has been a significant problem in Medicine in general and Urology in particular for decades. The formation of a biofilm typically consists of multiple, defined steps: First, a so-called conditioning film forms within minutes after insertion of the foreign body. Here, various constituents from urine, blood and surrounding tissues such as polysaccharides, ions and glycoproteins deposit to the surface of the stent. Hence, the surface properties of the foreign body are altered, which enables planktonic bacteria to adhere to the conditioning film [4–6].

Studies have shown that around 42–100% of all indwelling ureteral stents are colonized by bacteria [7–9]. Typically, the bacteria continue to form a more mature biofilm as large, structured communities of bacteria adhere onto surfaces and secrete polysaccharides, nucleic acids, lipids and proteins that form an eminently protective cast around the bacteria. Bacteria manage to survive and proliferate in an otherwise hostile environment by enriching the matrix around them with DNA, proteins, and other organic material [10]. Also, the extracellular matrices shield bacteria from shear stress caused by urine flow, as well as from antibiotics [11, 12]. Other contributing factors to antibiotic resistance are the change in phenotype as bacteria transform from planktonic into stationary, biofilm-forming bugs and the tendency to slow down their metabolism hence evading antibiotic mechanisms of action [5].

Biofilm formation on ureteral stents is assumed to be initiated within minutes after insertion and has been proven to be established as early as 24 h after insertion [7]. In a study by Shabeena et al., longer indwelling times correlated with higher colonization rates and after 120 days, 90% of the stents were colonized [13]. Despite our knowledge of bacterial colonization and biofilm formation, the link to clinically significant urinary tract infections is poorly understood: even though most indwelling stents are colonized with bacteria, few patients with stents and positive urine cultures develop clinical symptoms. The complex interaction between the pathogen, the foreign body surface, and the host is the subject of numerous studies attempting to elucidate the problem. Altunali et al. prospectively evaluated 60 patients after ureteral stent placement and detected a clinically significant urinary tract infection in 11% of patients with a median follow-up of 111 days [14].

Recently, Salari et al. retrospectively investigated the link between urine culture, stent culture, and subsequent urinary tract infections. Of the 159 patients included in this study, 15% had positive urine and 45% had positive stent culture. Two-thirds of the patients with a positive stent culture had a negative urine culture. The calculated odds for patients with negative urine and positive stent culture were 5.7 and

13.6 for patients with both cultures positive to develop a urinary tract infection in the future, respectively [15].

3 Encrustation

Encrustation describes the process of mineral crystal deposition on the surfaces of a foreign body. Biofilm formation and encrustation are believed to be interdependent processes, with bacterial colonization being addressed as the primary culprit for both events.

Clinically, we often see markedly encrusted proximal and distal ends of ureteral stents, with the mid-section typically being unconcerned and the last part of the stent to encrust. Researchers hypothesized that a kind of “wiping” effect of ureteral peristalsis and that the curled proximal and distal ends are continually exposed to urine, and its contents might be responsible for this phenomenon [16]. In Fig. 1, an encrusted catheter harvested from a mouse bladder after 6-day dwelling time from our catheter-associated urinary tract infection mouse model is depicted.

As previously described, ureteral stents are almost instantaneously coated with a conditioning film of glycoproteins, polysaccharides and ions upon introduction in the urinary tract. From there, the fate of the indwelling stent depends on several factors, which can either leave the stent unchanged, initiate the formation of a biofilm or cause encrustation of the stent [3, 17, 18]. However, these different entities might



Fig. 1 Macroscopic appearance of catheter encrustation and stone formation after 6-day dwelling time. Biofilm and calculi were particularly noted on catheter lateral ends [42]

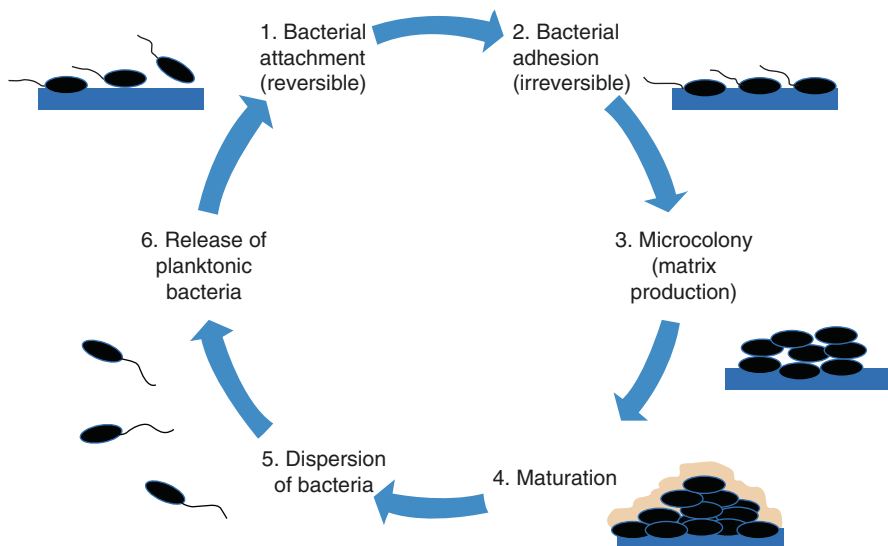


Fig. 2 The process of biofilm formation [41]

be encountered on the same stent and exist simultaneously. That being said, a biofilm with its exopolysaccharide matrix might serve as a scaffold for mineral crystals to be retained, hence serving as a nidus for encrustation. Conversely, crystals deposited on the conditioning film enlarge the surface enormously, thus facilitating bacterial adherence. A simplified depiction of the process of biofilm formation in shows in Fig. 2.

Large crystals can form rapidly with urease-positive bacteria, especially *Proteus mirabilis*, and cause significant problems in affected patients. These Gram-negative bacteria are notorious for their ability to form large infection stones in the urinary tract via elevation of the urine pH. An alkaline pH is essential, as struvite precipitates above a pH level of 7.2 [19]. With the enzyme urease, urea in urine is split into ammonia and CO_2 . Because of high ammonia and CO_2 levels and the reaction of CO_2 with H_2O , which results in high bicarbonate levels, the pH level steadily rises and plateaus finally at 7.2–8.0. Ammonia continues to be hydrolyzed to form ammonia ions. Subsequently, “struvite-apatite dust” is formed around the urease-producing bacteria. Both in and around these bacteria, crystallization may develop and lead to crystal formation and finally encrustation. Urease positive bacteria tend to cause severe encrustation that often results in device failure with obstruction, leading to hydronephrosis and possibly urosepsis [20].

4 Risk Factors for Encrustation

Several risk factors, such as indwelling time, bacterial colonization, comorbidity of the patient, and the physical properties of the ureteral stent that lead to encrustation, have been established.

As with biofilm formation, studies have shown that with longer indwelling times, encrustation tends to increase. El-Fatih et al. showed that 9% of stents had encrustations after an indwelling time of 6 weeks, 48% of patients after 6–12 weeks and 77% after 12 weeks [21]. Kawahara and colleagues evaluated 330 ureteral stents for encrustation and found 47% encrusted. A time-dependent encrustation rate was evident where 27% of stents with an indwelling time of fewer than 6 weeks showed encrustations. However, this rate increased to 57% after 6–12 weeks and 76% after more than 12 weeks. Their study could also demonstrate a correlation with ureteral stent size as higher rates of encrustation in ureteral catheter 6F or smaller were seen compared to 7F stents [22]. Kartal and coworkers came to the same conclusion in their study in 2018 that prolonged indwelling time in patients with stents and urolithiasis was associated with increased encrustation and stone burden [23].

Regarding patient-specific factors, diabetes mellitus, recurrent urinary tract infections, and chronic renal failure have shown to increase the risk of bacteriuria and possibly stent encrustation [24].

5 Strategies to Avoid Stent Encrustation

The complex nature of stent encrustation is reflected in the ubiquity of encrustations regardless of the stent materials used. There is a great incentive for companies to push advances in the field as the global ureteral stent market size was estimated at USD 422.9 million in 2019. However, due to the rise in urological and kidney-related diseases, the market is still growing and is expected to reach USD 723.6 million in 2027 [25].

Innovations that have been explored to diminish complications of ureteral stenting involve coating with antimicrobials, altering the material compounds or changing the stent architecture.

Today, most stents used in everyday practice are comprised of polymer blends. The majority of these stents are coated with bioactive compounds. However, the exact composition is unknown as these blends are typically proprietary.

5.1 Stent Coating

Several attempts have been made to develop stent coatings that prevent biofilm formation and encrustation. Initial attempts to coat ureteral stents with antibiotic agents have been abandoned due to high rates of antibiotic resistance and failed efficacy in clinical trials [26]. Another substance that has been investigated for its potential to prevent biofilm formation was heparin. For decades, this negatively charged glycosaminoglycan has been extensively used as an anticoagulant and was hypothesized to hamper bacterial adhesion and biofilm formation. However, the data for heparin are ambiguous as some authors found significantly decreased encrustation in

heparin-coated stents as others failed to demonstrate a benefit [27, 28]. In a recently published work, Soria et al. tested a new heparin-coated biodegradable antireflux stent (BraidStent[®]-H) in a porcine model [29]. The newly developed stent could demonstrate an early decrease in bacterial load, but this effect did not prevail long-term.

5.2 *Metal Stents*

Metal-based stents have been introduced to tackle some of the significant drawbacks of polymer stents, such as encrustation, device failure resulting from external compression and the need for regular stent change. Various models with different mechanisms of action are currently on the market.

Resonance[®] (Cook Medical, USA) is a metal-based double-J stent composed of a proprietary nickel–cobalt chromium–molybdenum alloy [30]. Unlike conventional polymer stents, this metal stent is not a hollow tube with multiple holes but consists of tightly wound coils that help maintain continuous drainage by allowing urine to flow in and out of the coils. The Resonance[®] stent has proven to be safe and effective: Patel et al. reported successful treatment of hydronephrosis in 96% of patients in their series with median indwelling times of 19.5 months in non-malignant and 12 months in malignant ureteral obstruction [31]. The recommended indwelling time of the Resonance[®] stent is 12 months, hence reducing the frequency of stent changes markedly and making it more cost-effective when compared to conventional polymer stents that must be changed every 3–6 months [32]. However, in a series with a longer follow-up, a failure rate of 28% due to pain, recurrent infections, stent migration, hematuria and encrustation was reported [33].

A different method of action is adopted by the Allium[®] ureteral stent (Allium Medical Solutions, Israel), a self-expanding large caliber stent (24–30 Fr in diameter) of a nitinol alloy which is covered by a proprietary polymer to avoid tissue ingrowth and encrustation. According to the manufacturer, these stents are intended for short- and long-term use with a recommended maximum indwelling time of 3 years. The nitinol stents come mounted on a 10 Fr delivery system for antegrade or retrograde insertion. Moskovitz et al. first published their results on 49 Allium[®] stents in 40 patients in 2013 [34]. They reported successful stent placement of the stent in all patients, and after a mean indwelling time of 17 months and a mean follow-up of 21 months, stent migration occurred in 14.2%, one stent was occluded, and an uncomplicated removal with no evidence of obstruction hereafter was performed in eight patients.

Memokath[™] (PNN Medical, Denmark) is a self-expanding stent comprised of a nickel-titanium alloy. The nickel content of Memokath[™] is very low and encased in an inactive protective layer of biocompatible titanium oxide, making it suitable for people with a nickel allergy. The stent is thermally malleable so that upon insertion, the stent needs to be flushed with heated saline (60 °C) to expand. Agrawal et al. reported on their outcomes of 74 stents inserted in 55 patients [35]. They experienced 3 early complications (urinary extravasation, failed expansion and equipment

failure) and 18 late complications, including stent migration in 13, stent encrustation in 2 and fungal infections in 3 patients. The authors concluded that the Memokath™ represents a valid alternative to conventional polymer stents with durable long-term relief from ureteric obstruction.

No prospective trials compare the various stents in patients with chronic ureteral obstruction. However, Khoo et al. recently reported on their single-center experience with the Resonance®, Allium® and Memokath-051™ stent [36]. Compared to the latter two, the Resonance® metallic ureteric stent showed superior functional stent survival. However, follow-up in this study was relatively short (median actual stent follow-up was less than 12 months for all stents), and the retrospective nature without randomization makes the study prone to selection bias.

In conclusion, metal stents represent viable alternatives for patients who require long-term stenting with comparatively low encrustation rates.

5.3 *Biodegradable Stents*

Biodegradable stents are ureteral stents that consist of materials that dissolve over time. This approach has several advantages as invasive removal is not required after the stents have completely dissolved over time. In addition, biodegradable materials tend to be softer, which may benefit stent tolerability and stent discomfort. Also, the ever-changing surface of the stent during dissolution might impede bacterial adhesion and encrustation. Various materials have been tested for this purpose, such as polyglycolic acid, polylactic acid, poly(lactic-co-glycolic acid) and alginate-based materials [3, 37, 38]. With some of the tested materials like polylactic acid, issues with incomplete degradation and biocompatibility prevented further development, while others showed promising preclinical utility but were not further investigated.

The Uriprene stent (Poly-Med, USA), comprised of a radiopaque, glycolic–lactic acid formula, is widely considered the most promising candidate for future clinical implementation. This degradable stent has the unique characteristic to degrade in the distal to proximal direction, which minimizes the risk of blocking fragments in the ureter and the time the renal coil could block the ureteropelvic junction. Experiments in porcine models have demonstrated good biocompatibility with less inflammation when compared to conventional non-degradable polymer stents. In a study by Chew et al., 90% of the stents were completely degraded after 4 weeks, and less hydronephrosis as compared to the biostable stents was observed [39].

The biodegradable stents could be beneficial in specific indications in the future, especially for patients after ureteroscopy and for short-term stenting. However, to date, there are no biodegradable stent solutions for long-term stenting on the horizon, which probably represent the patient cohort that suffers most from stent encrustation and its sequelae.

6 Conclusions

Due to the complex biology and interactions between foreign body surfaces, the host and microbes, a simple, one-fits-all solution is not very likely to be developed. Nonetheless, our knowledge of the underlying biology has dramatically expanded, and novel technologies are being tested. Probably the easiest solution is to appraise ureteral stenting critically and omit stenting whenever feasible. However, for patients in need of a ureteral stent the future might bring “ideal” stents that are biodegradable, coated to avoid biofilm formation and encrustation and ideally emit sufficient levels of specific drugs that prevent tissue ingrowth or even dissolve urinary calculi [40–42].

Key Points

- Ureteral stent encrustation is a significant problem in the field of Urology.
- Most ureteral stents to date are made of a polymer blend with a proprietary coating.
- Attempts have been made to reduce biofilm formation and encrustation via altering the stent surface, architecture and design.
- Biodegradable stents may help avoid the forgotten stent syndrome, especially in patients after endourologic procedures.
- For patients with malignant obstruction, metal stents have proven as a viable alternative to the conventional polymer stents with less encrustation.

References

1. Zimskind PD, Fetter TR, Wilkerson JL. Clinical use of long-term indwelling silicone rubber ureteral splints inserted cystoscopically. *J Urol.* 1967;97:840–4.
2. Finney RP. Experience with new double J ureteral catheter stent. *J Urol.* 1978;120:678–81.
3. Lange D, Bidnur S, Hoag N, et al. Ureteral stent-associated complications—where we are and where we are going. *Nat Rev Urol.* 2015;12:17–25.
4. Costerton JW. Introduction to biofilm. *Int J Antimicrob Agents.* 1999;11:217–21.
5. Tenke P, Kovacs B, Jäckel M, et al. The role of biofilm infection in urology. *World J Urol.* 2006;24:13.
6. Elwood CN, Lo J, Chou E, et al. Understanding urinary conditioning film components on ureteral stents: profiling protein components and evaluating their role in bacterial colonization. *Biofouling.* 2013;29:1115–22.
7. Reid G, Denstedt JD, Kang YS, et al. Microbial adhesion and biofilm formation on ureteral stents in vitro and in vivo. *J Urol.* 1992;148:1592–4.
8. Riedl CR, Plas E, Hübner WA, et al. Bacterial colonization of ureteral stents. *Eur Urol.* 1999;36:53–9.
9. Kehinde EO, Rotimi VO, Al-Hunayan A, et al. Bacteriology of urinary tract infection associated with indwelling J ureteral stents. *J Endourol.* 2004;18:891–6.
10. Tenke P, Köves B, Nagy K, et al. Update on biofilm infections in the urinary tract. *World J Urol.* 2012;30:51–7.
11. Sutherland IWY. Biofilm exopolysaccharides: a strong and sticky framework. *Microbiology.* 2001;147:3–9.

12. Stewart PS, Costerton JW. Antibiotic resistance of bacteria in biofilms. *Lancet*. 2001;358:135–8.
13. Shabeena KS, Bhargava R, Manzoor MAP, et al. Characteristics of bacterial colonization after indwelling double-J ureteral stents for different time duration. *Urol Ann*. 2018;10:71–5.
14. Altunal N, Willke A, Hamzaoglu O. Ureteral stent infections: a prospective study. *Braz J Infect Dis*. 2017;21:361–4.
15. Salari B, Khalid M, Ivan S, et al. Urine versus stent cultures and clinical UTIs. *Int Urol Nephrol*. 2021;53:2237–42.
16. Singh I, Gupta NP, Hemal AK, et al. Severely encrusted polyurethane ureteral stents: management and analysis of potential risk factors. *Urology*. 2001;58:526–31.
17. Gristina AG. Biomaterial-centered infection: microbial adhesion versus tissue integration. *Science*. 1987;237:1588–95.
18. Tomer N, Garden E, Small A, et al. Ureteral stent encrustation: epidemiology, pathophysiology, management and current technology. *J Urol*. 2021;205:68–77.
19. Schwartz BF, Stoller ML. Nonsurgical management of infection-related renal calculi. *Urol Clin N Am*. 1999;26:765–78.
20. Flannigan R, Choy WH, Chew B, et al. Renal struvite stones—pathogenesis, microbiology, and management strategies. *Nat Rev Urol*. 2014;11:333–41.
21. el-Faqih SR, Shamsuddin AB, Chakrabarti A, et al. Polyurethane internal ureteral stents in treatment of stone patients: morbidity related to indwelling times. *J Urol*. 1991;146:1487–91.
22. Kawahara T, Ito H, Terao H, et al. Ureteral stent encrustation, incrustation, and coloring: morbidity related to indwelling times. *J Endourol*. 2012;26:178–82.
23. Kartal IG, Baylan B, Gok A, et al. The association of encrustation and ureteral stent indwelling time in urolithiasis and KUB grading system. *Urol J*. 2018;15:323–8.
24. Akay AF, Aflay U, Gedik A, et al. Risk factors for lower urinary tract infection and bacterial stent colonization in patients with a double J ureteral stent. *Int Urol Nephrol*. 2007;39:95–8.
25. Anon: Ureteral Stents Market Size | Industry Report, 2020–2027. <https://www.grandviewresearch.com/industry-analysis/ureteral-stents-market>. Accessed 30 Nov 2021.
26. El-Nahas AR, Lachine M, Elsayy E, et al. A randomized controlled trial comparing antimicrobial (silver sulfadiazine)-coated ureteral stents with non-coated stents. *Scand J Urol*. 2018;52:76–80.
27. Riedl CR, Witkowski M, Plas E, et al. Heparin coating reduces encrustation of ureteral stents: a preliminary report. *Int J Antimicrob Agents*. 2002;19:507–10.
28. Lange D, Elwood CN, Choi K, et al. Uropathogen interaction with the surface of urological stents using different surface properties. *J Urol*. 2009;182:1194–200.
29. Soria F, de La Cruz JE, Fernandez T, et al. Heparin coating in biodegradable ureteral stents does not decrease bacterial colonization-assessment in ureteral stricture endourological treatment in animal model. *Transl Androl Urol*. 2021;10:1700–10.
30. Anon: Resonance® Metallic Ureteral Stent Set | Cook Medical. https://www.cookmedical.com/products/uro_rmsr_webds/, https://www.cookmedical.com/products/uro_rmsr_webds/. Accessed 01 Dec 2021.
31. Patel C, Loughran D, Jones R, et al. The resonance® metallic ureteric stent in the treatment of chronic ureteric obstruction: a safety and efficacy analysis from a contemporary clinical series. *BMC Urol*. 2017;17:16.
32. López-Huertas HL, Polcari AJ, Acosta-Miranda A, et al. Metallic ureteral stents: a cost-effective method of managing benign upper tract obstruction. *J Endourol*. 2010;24:483–5.
33. Kadlec AO, Ellimoottil CS, Greco KA, et al. Five-year experience with metallic stents for chronic ureteral obstruction. *J Urol*. 2013;190:937–41.
34. Moskovitz B, Halachmi S, Nativ O. A new self-expanding, large-caliber ureteral stent: results of a multicenter experience. *J Endourol*. 2012;26:1523–7.
35. Agrawal S, Brown CT, Bellamy EA, et al. The thermo-expandable metallic ureteric stent: an 11-year follow-up. *BJU Int*. 2009;103:372–6.
36. Khoo CC, Ho C, Palaniappan V, et al. Single-centre experience with three metallic ureteric stents (Allium® URS, Memokath™-051 and Resonance®) for chronic ureteric obstruction. *J Endourol*. 2021;35(12):1829–37.

37. Lingeman JE, Schulsinger DA, Kuo RL. Phase I trial of a temporary ureteral drainage stent. *J Endourol.* 2003;17:169–71.
38. Chew BH, Lange D, Paterson RF, et al. Next generation biodegradable ureteral stent in a Yucatan pig model. *J Urol.* 2010;183:765–71.
39. Chew BH, Paterson RF, Clinkscales KW, et al. In vivo evaluation of the third generation biodegradable stent: a novel approach to avoiding the forgotten stent syndrome. *J Urol.* 2013;189:719–25.
40. Venkatesan N, Shroff S, Jayachandran K, et al. Polymers as ureteral stents. *J Endourol.* 2010;24:191–8.
41. Khoddami S, Chew BH, Lange D. Problems and solutions of stent biofilm and encrustations: a review of literature. *Turk J Urol.* 2020;46:S11–8. <https://doi.org/10.5152/tud.2020.20408>.
42. Janssen C, Lo J, Jager W, et al. A high throughput, minimally invasive, ultrasound guided model for the study of catheter associated urinary tract infections and device encrustation in mice. *J Urol.* 2014;192:1856–63. <https://doi.org/10.1016/j.juro.2014.05.0922>.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

