Heterogeneities in biofilms from clinical isolates under flow conditions

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Pancreatic cancer is the fourth leading cause of cancer death worldwide. The most common sign of presentation of pancreatic cancer is obstructive jaundice, which prevents the drainage of bile into the intestines and it is often associated with decreased survival in patients. Nowadays more than 70% of the patients with biliary obstructive jaundice is treated by biliary stenting; however, biliary stenting disrupts the natural anatomic barrier between the biliary and the gastrointestinal tract, strongly increasing the risk of a bacterial infection. Moreover, duodenal bacteria, by gaining access into the biliary system, can adhere to the stent surface and develop biofilms. Nevertheless, very little is known about the growth of biofilms on the stents and their role in infectious post-operative complications. In particular, the biliary system is an inherently fluid mechanical environment, where the gallbladder provides the driving pressure and the flow rate of the bile going through the ducts depends on the resistance between the gallbladder and the downstream end of the common bile duct. The average flow rate of the bile ranges between approximately 0.5 to 5 ml/min, which depends if the body is fasting or after a meal; this flow rate then corresponds – in the case for example of plastic stents, which are typically 2-4 mm in luminal diameter – to a maximum flow velocity of about 1-40 mm/s and to a shear rate at the inner surface of the stent of 1-80 s⁻¹. Therefore, the mechanical stress induced by the bile flow in the stent is likely to play a significant role in the formation of biofilms, as shown by our data. Six clinically relevant isolates from preoperative biliary stents were selected to be grown inside microfluidic channels at different flow rates, in which bacterial attachment and biofilm dynamics were recorded and quantified. We found that fluid flow largely influences biofilm morphology in all the isolates, for which the conditions of flow and shear stress that trigger heterogeneities in biofilm structure have been determined. These results will help us to improve our understanding of biofilm formation in the presence of fluid dynamic environments and eventually consider optimal parameters of flow in the design of medical devices.