

Compatibility of Irinotecan-loaded DC Bead™ with different volumes and types of nonionic contrast media

EAHP

Hamburg,
25-27 MarchI. Sarakbi
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Introduction

Irinotecan is a topoisomerase I inhibitor used for transarterial chemoembolization of liver metastases in patients with colorectal cancer. Because of its cationic properties it can be loaded to negatively charged DC Bead™ microspheres, which possess the ability to load and release irinotecan in a controlled manner. Prior to administration, the loaded beads are mixed with non-ionic contrast medium to guide the injection. The aim of the study was to evaluate the compatibility of irinotecan-loaded DC Bead™ (bead size M1, 70-150 µm) with different types and volumes of non-ionic contrast media over a maximum period of 24 hours and storage at room temperature.

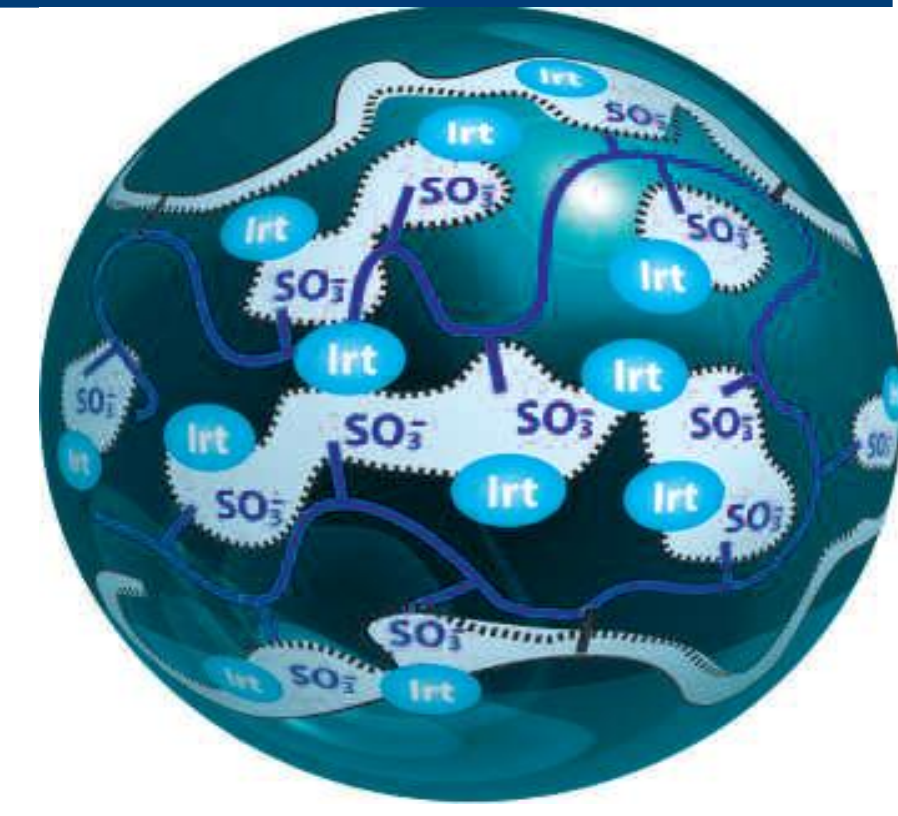


Fig. 1 Irinotecan-loaded DC Bead™

Material and Methods

Loading of test suspensions

2 mL DC Bead™ M1 with 100 mg irinotecan within 2 hours
The loading efficiency was determined by measuring the concentrations of irinotecan in samples of the excess solutions via a RP-HPLC assay with UV detection. The samples were diluted 1:4 with 0.9% NaCl solution and acidified with 10 µl 1% H₃PO₄ to pH 3.5.

Compatibility tests

IEBs were mixed with up to four different volumes, i.e. 5, 10, 20, 30 mL of seven nonionic contrast media: Accupaque™ 350, Imeron® 400 MCT, Optiray™ 300, Optiray™ 350, Solutrast® 350, Ultravist® 370, Xenetix® 350 and stored light-protected at room temperature over a period of 24 h. Samples were taken after 30, 60, 120, 240, 480, and 1440 min. The concentrations of eluted irinotecan were measured in triplicate by RP-HPLC.

HPLC-method

Waters HPLC system: 717 plus autosampler, 510 HPLC-pump, PDA detector 996
Detection wavelength: 225 nm
Column: PerfectChrom 100CN, 250 mm*4.6 mm, particle size 5 mm .
Mobile Phase:
75% 0.02 M KH₂PO₄ solution
+ 25% acetonitrile
Flow rate: 1 ml/min
Inject. volume: 20 µl
Run time: 15 min
Software:
Waters Empower Pro

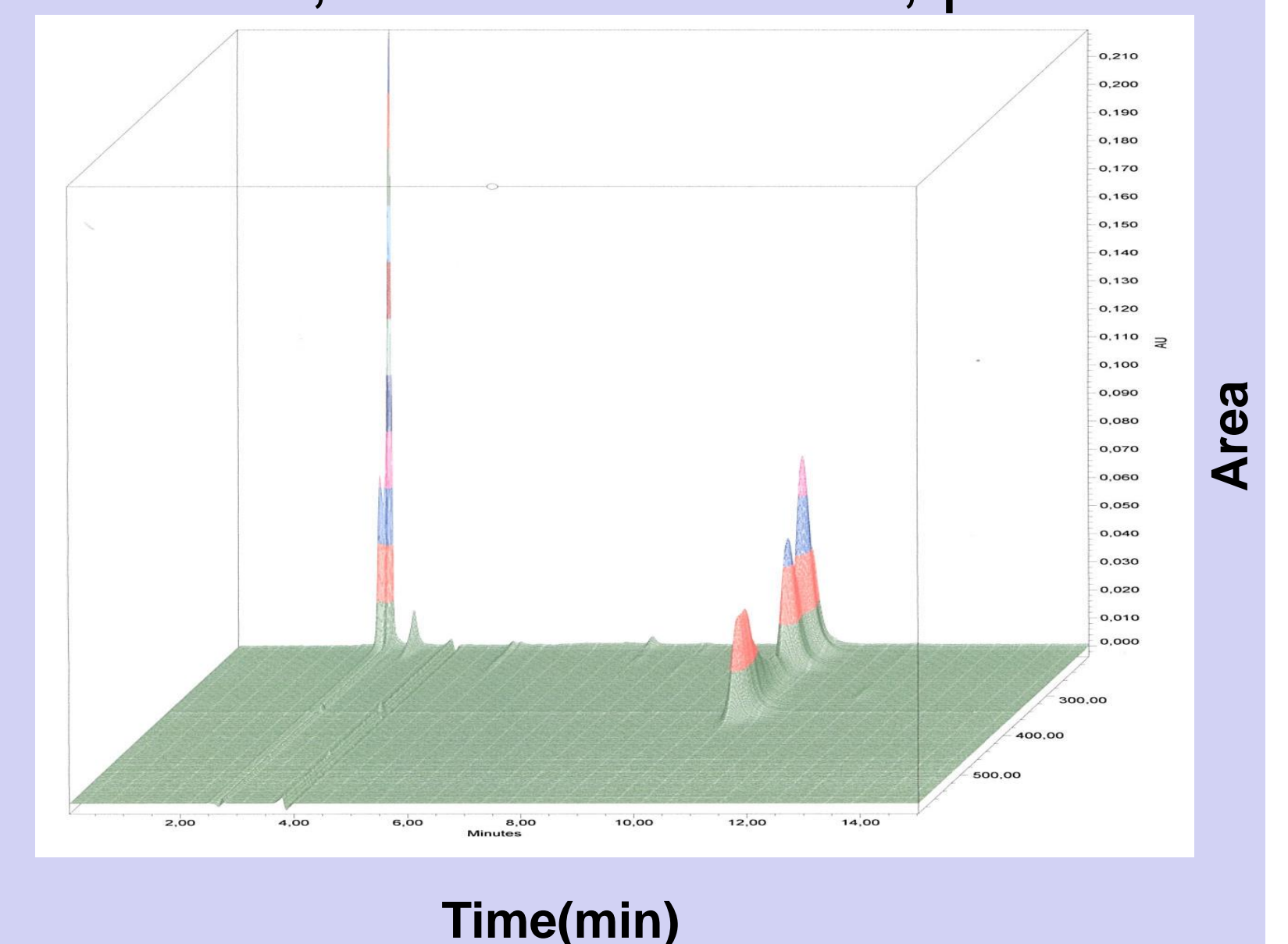


Fig.2 HPLC chromatogram of irinotecan

Results

Mixing of IEB (bead size M1) with nonionic contrast media decreased the irinotecan loading efficiency between minimum 2.5% and maximum 18% over the observation period of 24 h (detailed results in Fig. 3-6).

The rate and amount of irinotecan eluted from the beads varied relying on the type and volume of contrast medium admixed. However, no further elution or degradation was observed after the initial rapid release.

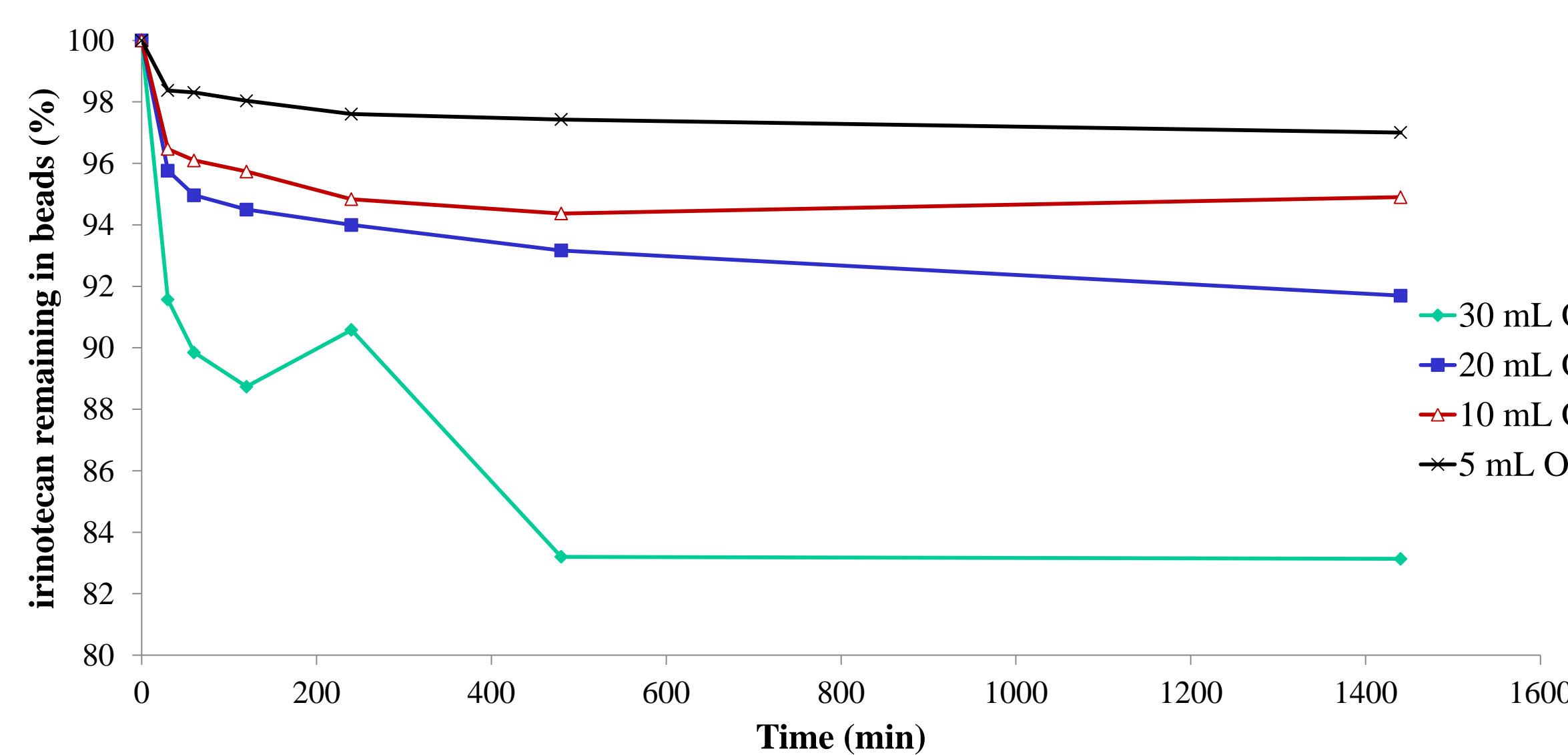


Fig. 3 Percentage rate [%] of irinotecan remaining loaded in DC BeadM1™ after mixing with different volumes of Optiray™ 300.

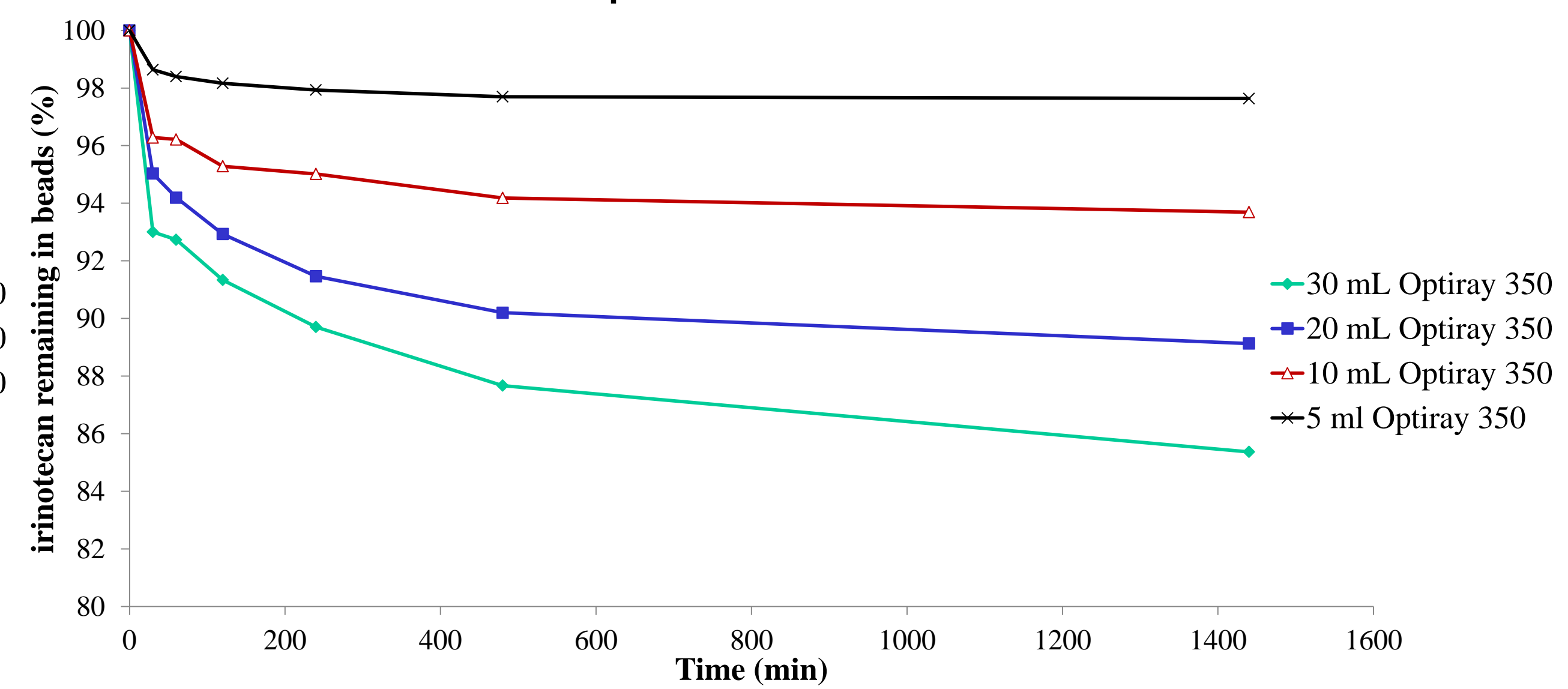


Fig 4 Percentage rate [%] of irinotecan remaining loaded in DC BeadM1™ after mixing with different volumes of Optiray™ 350

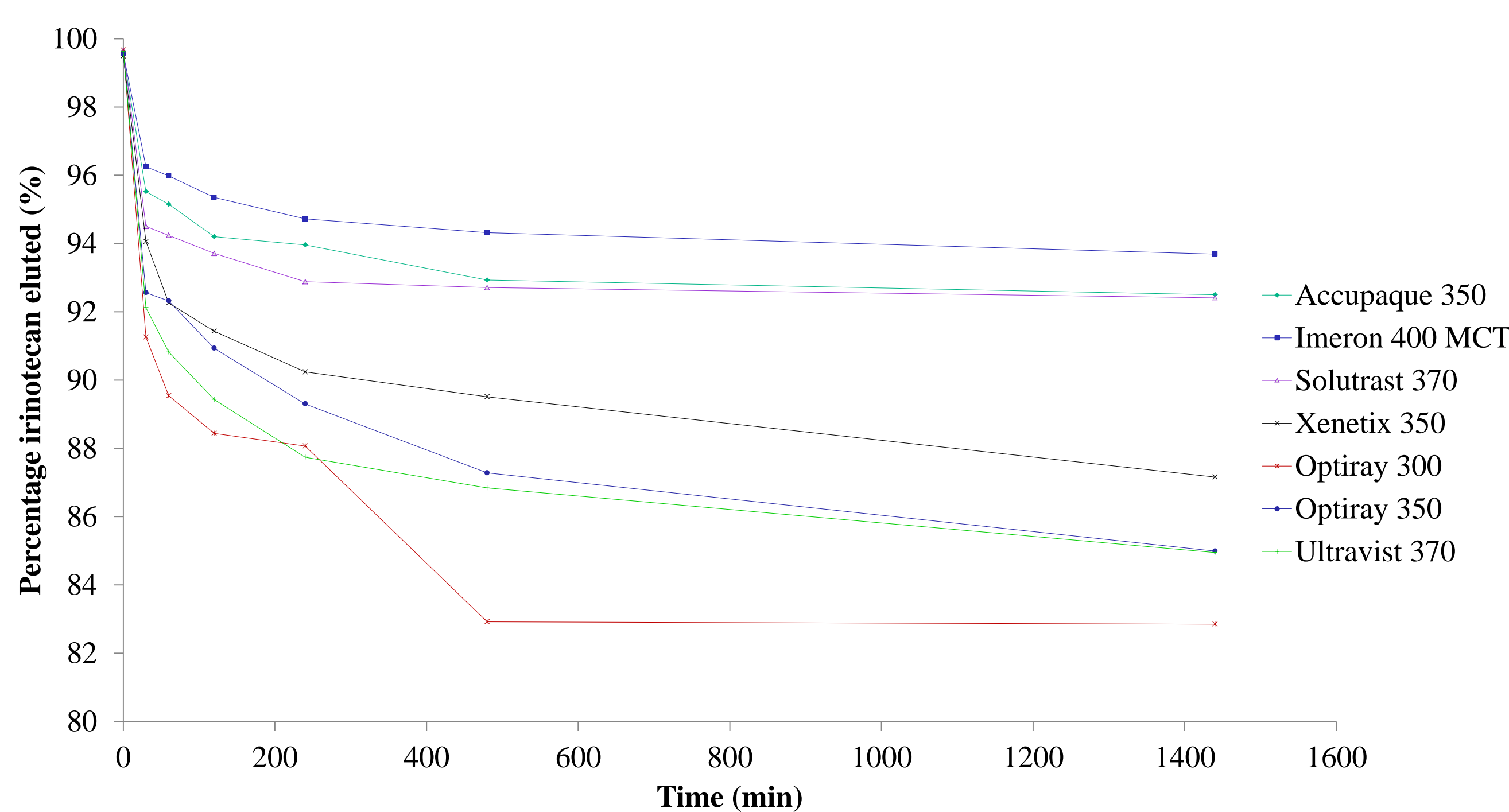


Fig 5 Percentage rate [%] of irinotecan remaining loaded in DC BeadM1™ after admixture with 30 mL of each contrast medium

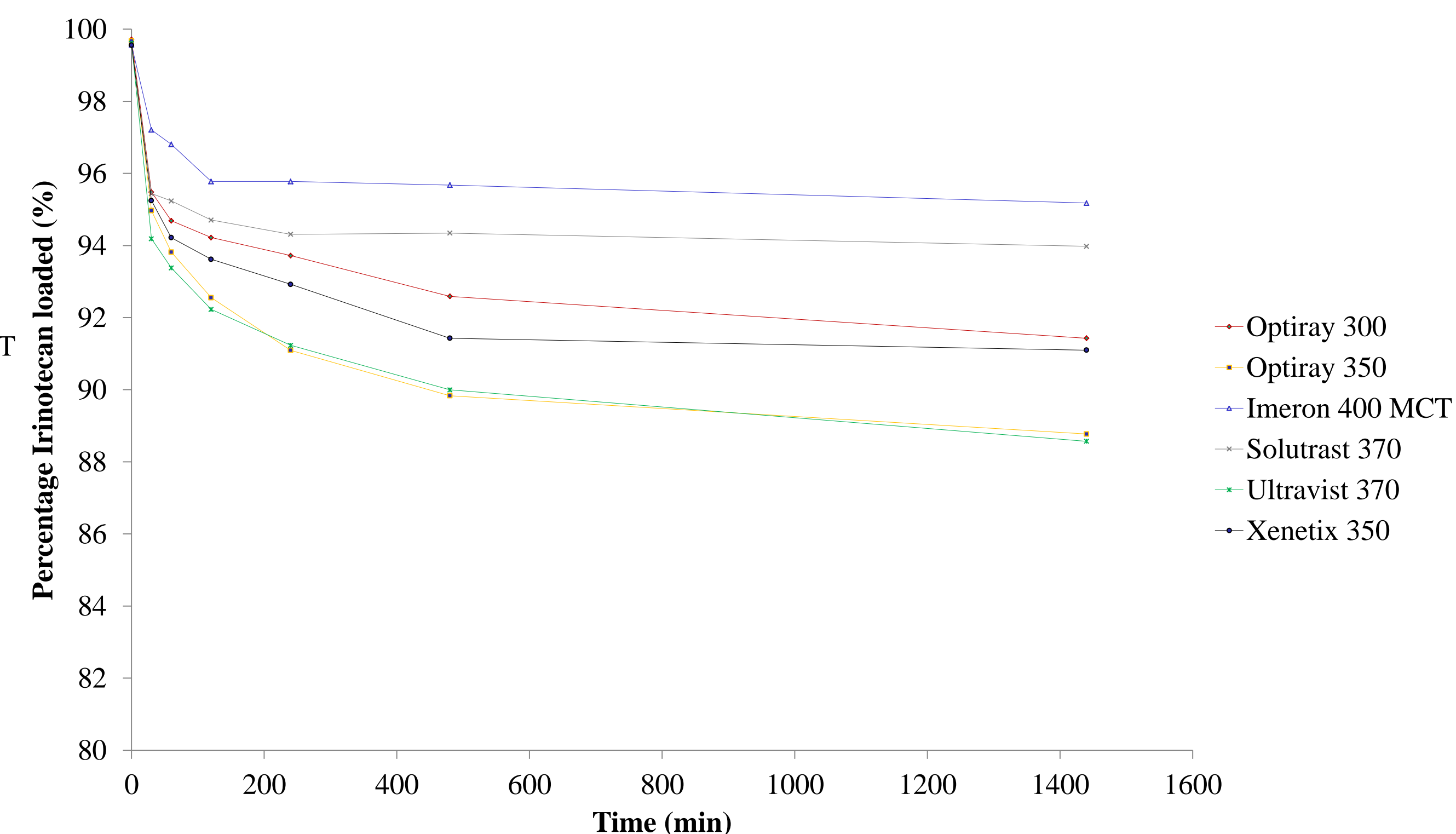


Fig 6 Percentage rate [%] of irinotecan remaining loaded in DC BeadM1™ after admixture with 20 mL of each contrast medium

Conclusion

Because of the initial rapid release (1-9 %) it is not recommendable to prepare the admixture of irinotecan-loaded beads with contrast medium in centralized cytotoxic preparation units in advance. Admixture should be performed by the physicians immediately prior to the delivery procedure.