

Supplementary material

Composite poly(DL-lactide-co-glycolide)/poly(acrylic acid)) hydrogels synthesized using UV and gamma irradiation: comparison of material properties

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The appearance of disk-shaped composite hydrogels synthesized using UV and gamma irradiation



Fig. S.1. Photograph of the composite hydrogels synthesized using UV irradiation (UV-PLGA-PAA). Sample shown on the left is air-dried, and sample shown on the right is swollen to equilibrium in phosphate-buffered saline (pH = 7.4 and $I = 0.154$ M).



Fig. S.2. Photograph of the composite hydrogels synthesized using gamma irradiation (G-PLGA-PAA). Sample shown on the left is air-dried, and sample shown on the right is swollen to equilibrium in phosphate-buffered saline (pH = 7.4 and $I = 0.154$ M).

FTIR-ATR examination of chemical composition uniformity within composite hydrogels synthesized using UV and gamma irradiation

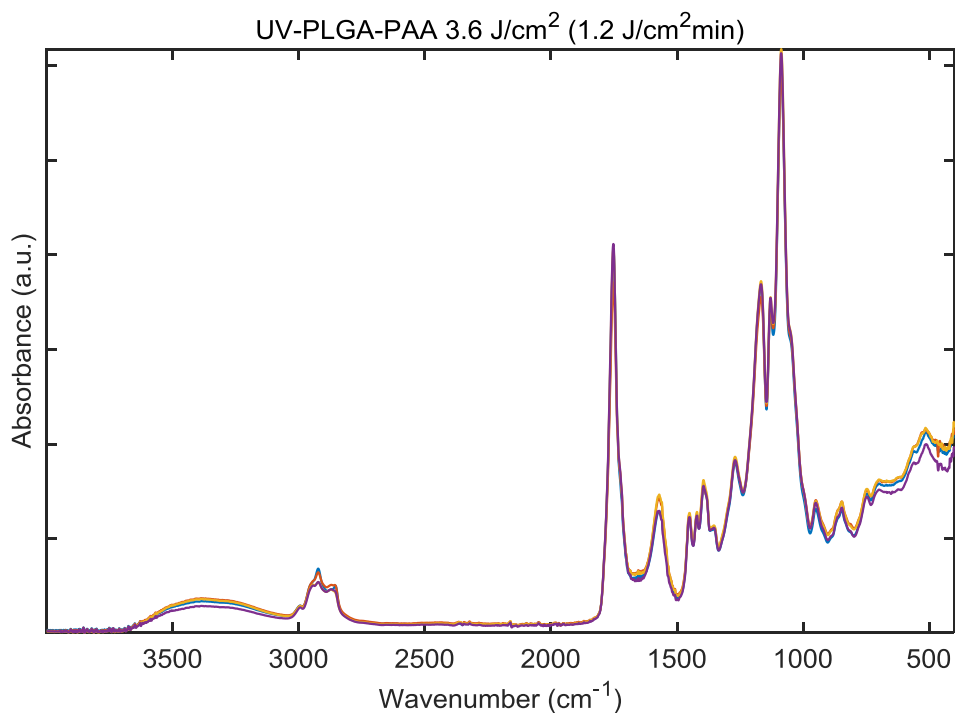


Fig. S.3. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using UV irradiation (UV-PLGA-PAA); dose: 3.6 J/cm²; dose rate 1.2 J/cm²min.

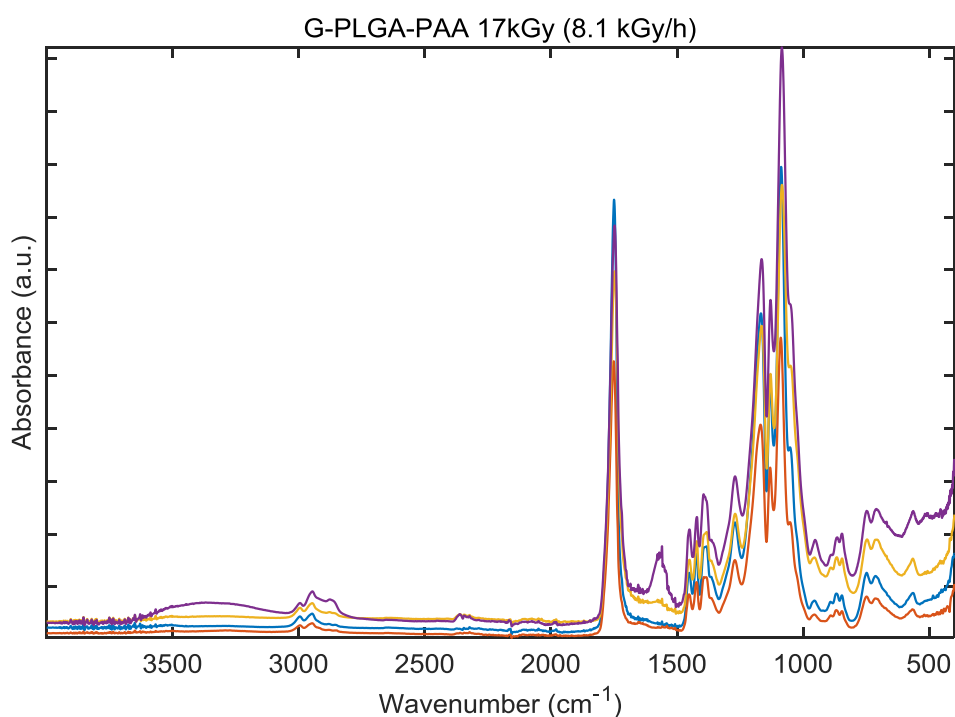


Fig. S.4. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using gamma irradiation (G-PLGA-PAA); dose: 17 kGy; dose rate: 8.1 kGy/h.

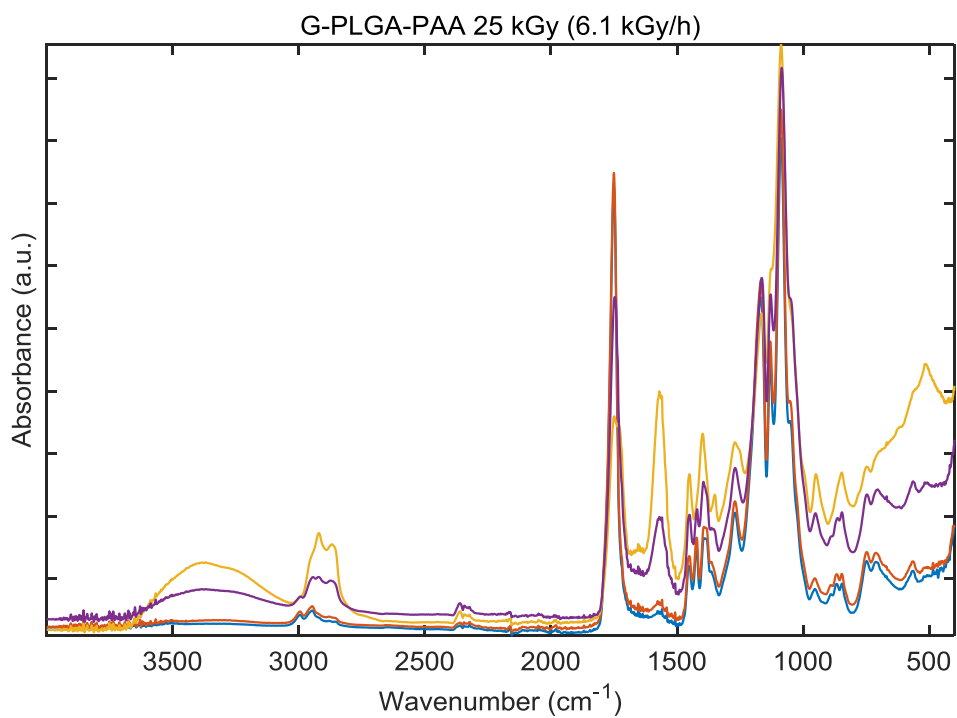


Fig. S.5. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using gamma irradiation (G-PLGA-PAA); dose: 25 kGy; dose rate: 6.1 kGy/h.

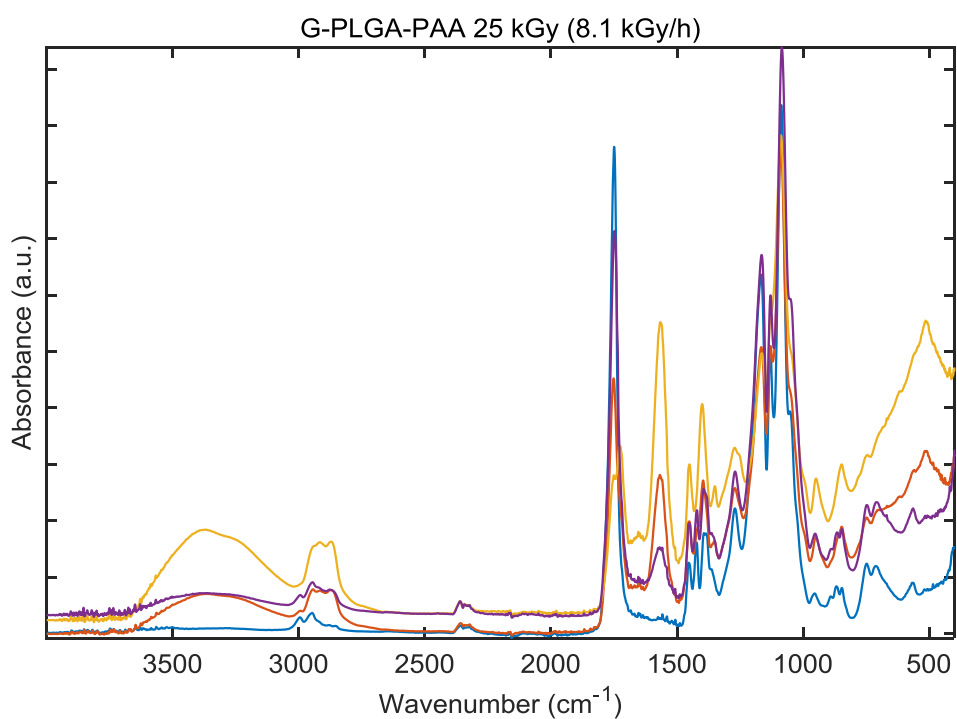


Fig. S.6. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using gamma irradiation (G-PLGA-PAA); dose: 25 kGy; dose rate: 8.1 kGy/h.

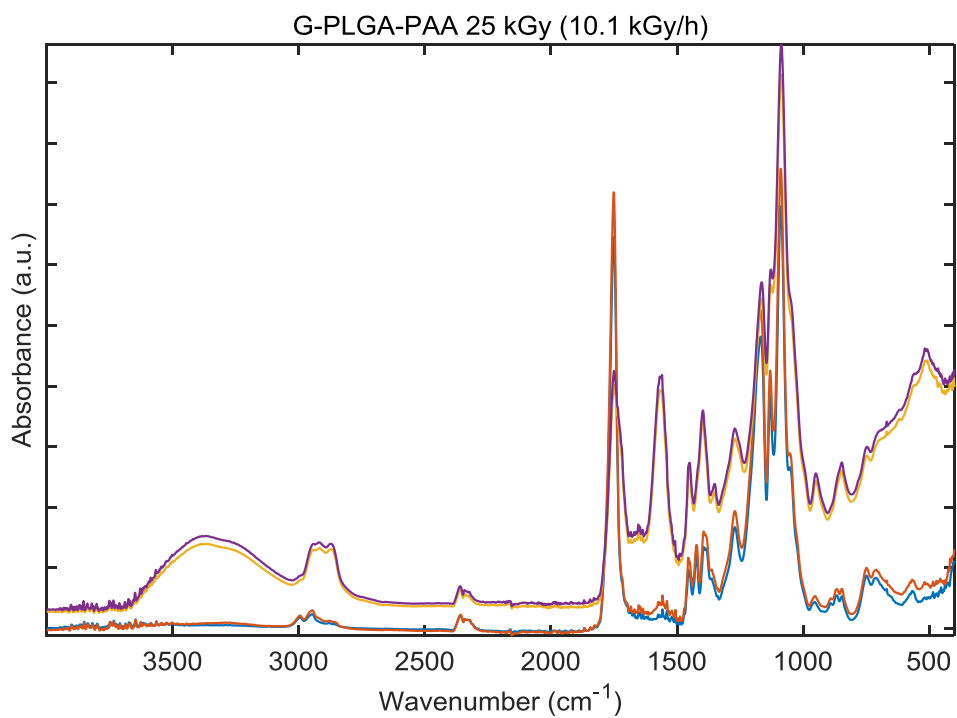


Fig. S.7. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using gamma irradiation (G-PLGA-PAA); dose: 25 kGy; dose rate: 10.1 kGy/h.

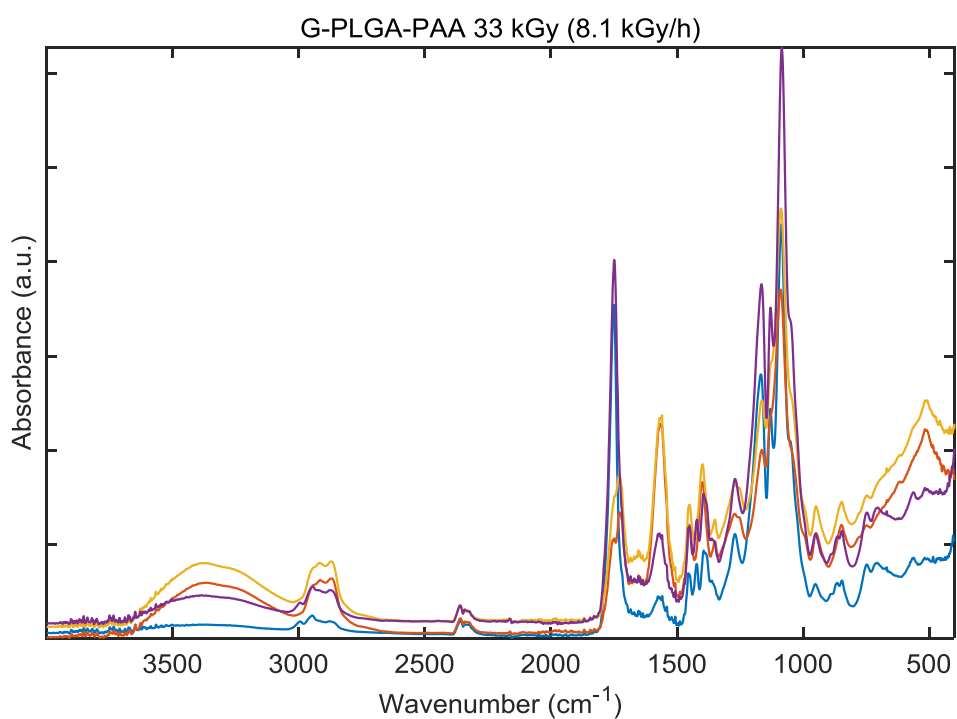


Fig. S.8. Raw FTIR-ATR spectra obtained at different locations within the dry composite hydrogel synthesized using gamma irradiation (G-PLGA-PAA); dose: 33 kGy; dose rate: 8.1 kGy/h.

Estimation of moisture content in solvent exchange dried composite hydrogels

We used a typical solvent exchange drying protocol under ambient conditions to minimize pore collapse and retain the initial microstructural features of composite hydrogels. It is difficult to completely avoid the presence of surface moisture in highly hydrophilic materials such as composite hydrogels containing PAA since they can absorb moisture rapidly during routine handling. Presence of PLGA in the composite also substantially limits the possibility of drying at elevated temperatures and drying under vacuum may change the initial microstructure.

To estimate the typical moisture content of composite PLGA-PAA hydrogel samples and their thermal stability, we performed simultaneous thermogravimetric measurement (TG) and differential thermal analysis (DTA). All TG and DTA experiments were carried out with the heating rate of 10 °C/min in air. **Fig. S.9** shows TG and DTA curves for the representative sample synthesized using the gamma irradiation dose of 25 kGy and a dose rate of 8.1 kGy/h. The event in the temperature region between 30 and 110 °C mainly corresponds to the evaporation of water. Hence, the moisture accounts for only several percent of the total sample mass. In order to estimate the upper bound of moisture content after solvent exchange drying, we recorded the TG and DTA curves for the dried hydrogel of pure crosslinked PAA synthesized using UV irradiation and identical experimental conditions as for the synthesis of composite PLGA-PAA hydrogels (see **Fig. S.10**). The mass loss due to water evaporation up to 110°C was approximately 6% and comparable to the mass loss in composite PLGA-PAA hydrogels. Our findings are similar to other results reported for pure dried PAA such as (Dubinsky et al., 2004).

We prepared all samples for DSC measurements simultaneously under the same conditions and later stored them in the same low-moisture ambient to minimize differences in moisture content. It is well-known that water can act as a plasticizer and reduce T_g , but the effect of variations in moisture content should be mostly compensated for during sample preparation. Hence, the measured shifts of T_g should be minimally affected. We also cannot aim for very high accuracy of T_g measurements for PLGA due to the presence of enthalpic relaxation peaks caused by the release of mechanical stresses imposed during the synthesis stage.

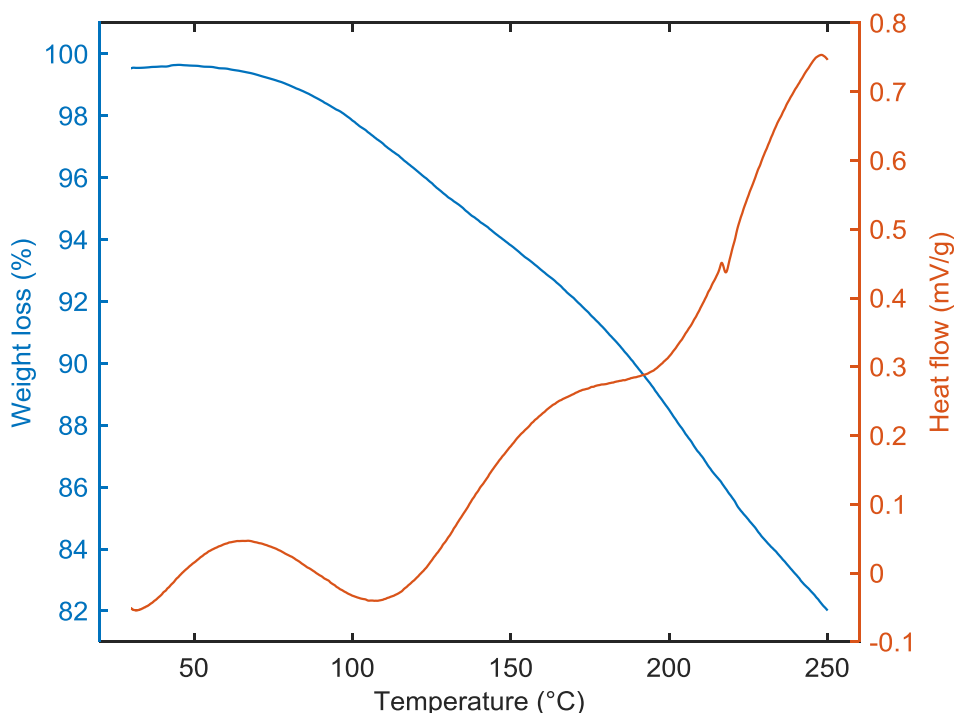


Fig. S.9. TG and DTA curves of the dried composite PLGA-PAA hydrogel synthesized using the gamma irradiation dose of 25 kGy and dose rate of 8.1 kGy/h.

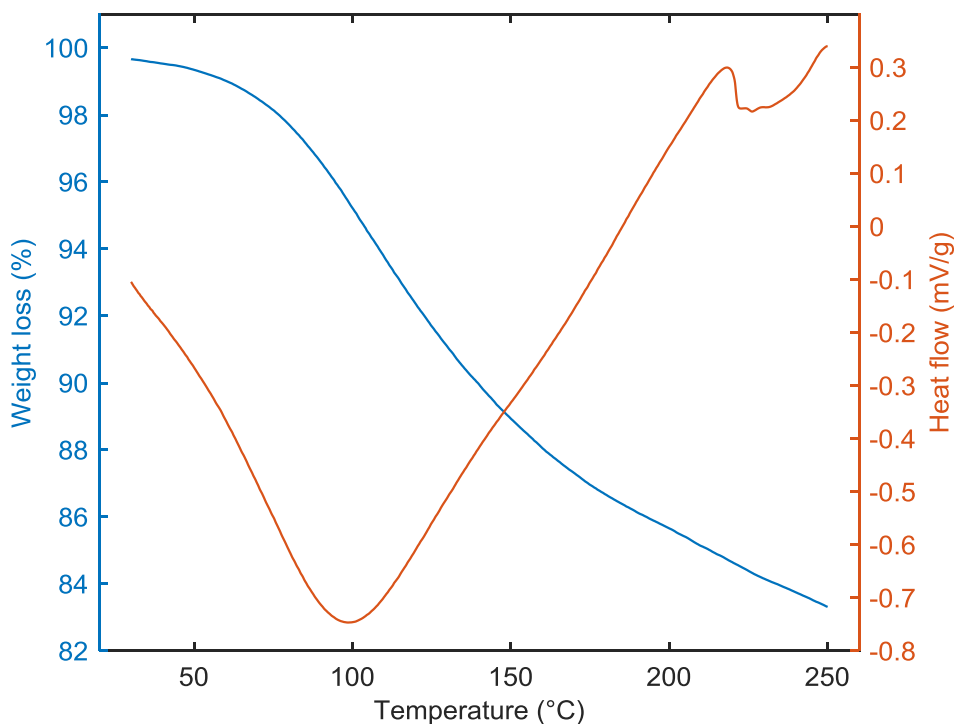


Fig. S.10. TG and DTA curves of the dried crosslinked PAA hydrogel synthesized using UV irradiation.

Analysis of the poly(acrylic acid) glass transition within composite hydrogels

Although one can expect to detect the T_g of pure atactic PAA homopolymer around 105 °C, the situation is quite different in our composite PLGA-PAA hydrogels. The main reason for the absence of the characteristic PAA glass transition should be the high degree of crosslinking. Crosslinks can restrict the motion of polymer main chains and impede the detection of T_g (Thürmer et al., 2014). The previous study showed that the glass transition of PAA may become undetectable when the gel is highly crosslinked using a multifunctional crosslinker (Greenberg and Kusy, 1980). Another possible reason can be the specific synthesis and drying protocol leading to the substantial shift of T_g towards higher temperatures. We dried the purified composite PLGA-PAA hydrogels equilibrated in PBS directly by the solvent exchange to retain the microstructural features and composition of synthesized samples as much as possible. The carboxyl groups within the PAA hydrogel deprotonate at pH = 7.4 and cation exchange occurs with the surrounding PBS medium that contains abundant sodium and potassium cations. Therefore, these cations remain trapped in the structure and neutralize PAA. In theory, we expect to find the glass transitions of such sodium and potassium neutralized PAA at higher temperatures and outside the recorded temperature range (approximately between 190 and 230 °C). We also expect for these glass transitions to overlap with the endothermic peak corresponding to thermal degradation of 50:50 PLGA that appears above 200 °C (D'Avila Carvalho Erbetta et al., 2012).

In order to investigate if the glass transition of PAA is likely to appear in our samples, we carried out the synthesis of pure crosslinked PAA (without the presence of PLGA in the initial solution) using UV irradiation and identical experimental conditions as for the synthesis of composite PLGA-PAA hydrogels. To examine the contribution of PAA neutralization in PBS, we performed the same synthesis using UV irradiation where the nonsolvent bath contained only distilled water. The obtained crosslinked PAA hydrogels were then dried according to the previously employed solvent exchange protocol.

Figs. S.11 and **S.12** show the obtained DSC thermograms during the first and second heating cycle with the heating rate of 10 °C/min under nitrogen purging. DSC thermograms of the second heating cycle in the

range from 55 to 200 °C are similar. They reveal good thermal stability and the glass transitions cannot be detected in the samples. Such results indicate the presence of a highly crosslinked structure. However, DSC thermograms in the first heating cycles differ in the pattern of water volatilization.

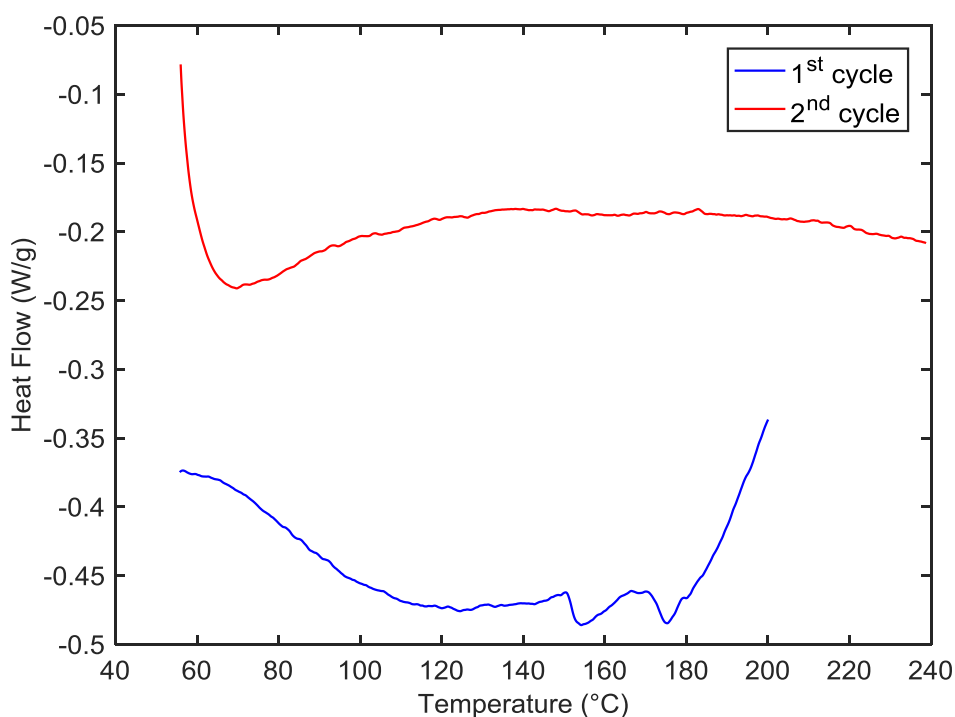


Fig. S.11. DSC thermograms of the dried crosslinked PAA hydrogel formed in PBS.

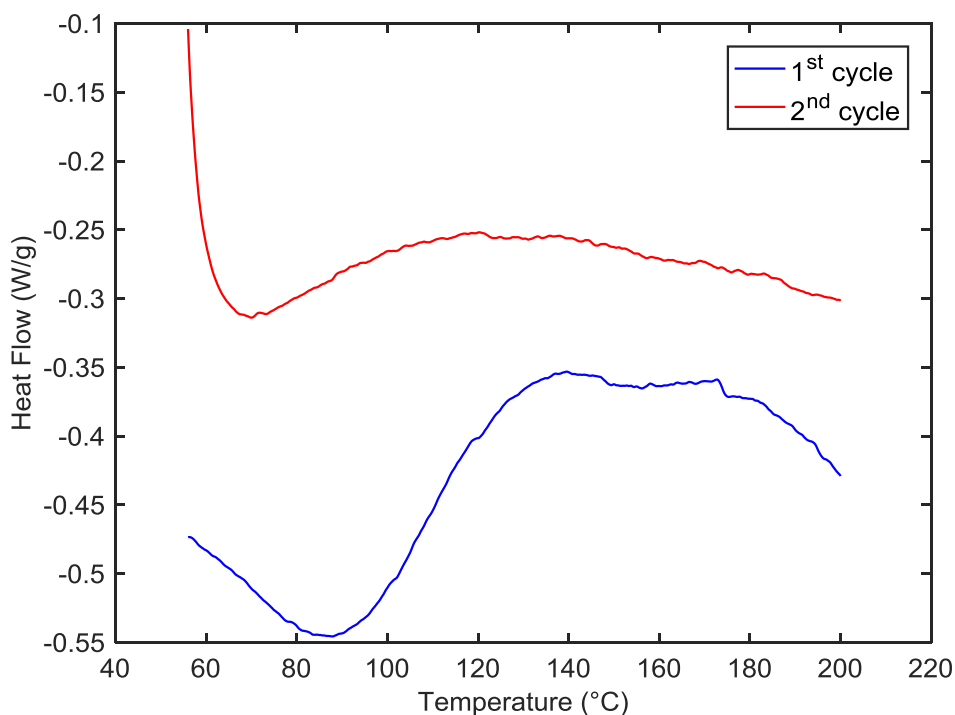


Fig. S.12. DSC thermograms of the dried crosslinked PAA hydrogel formed in distilled water.

Dehydration occurs dominantly at lower temperatures for the PAA hydrogel formed in distilled water. Conversely, dehydration occurs at a lower rate with temperature increase for PAA hydrogels formed in PBS. In addition, two endothermic peaks corresponding to the elimination of bound water appear at the approximate temperatures of 155 and 175 °C. These endothermic peaks probably correspond to relaxations

of PAA chains neutralized with sodium and potassium cations due to bound water release. Hence, the cations from PBS medium mainly contribute by retarding water elimination from the hydrogel.

According to the results of DSC characterization for pure PAA, we cannot expect to detect the T_g of PAA in the composite PLGA-PAA hydrogels. If this is the case, the origin of DSC events at temperatures above 60 °C needs to be clarified and we propose here the interpretation relying on additional measurements.

Minor endothermic events and slight baseline shifts in the DSC thermograms shown in **Fig. 3** at temperatures above approximately 60 °C can be ascribed to the volatilization of weakly bound or adsorbed water mostly present in the sample as residual surface moisture. However, more notable endothermic peaks (including the ones above 100 °C) correspond to the evaporation of strongly bound water trapped within the chains of PAA and the possible formation of anhydride involving less reactive carboxyl groups. Up to 150 °C, the PAA degrades mainly through the elimination of water and formation of anhydride groups (McGaugh and Kottle, 1967). More detailed characterization of such DSC events in different PAA molecules can be found in the studies of Maurer and coworkers such as (Maurer et al., 1987). The processes of water volatilization and anhydride formation are especially prominent in the composite PLGA-PAA hydrogel synthesized using the gamma irradiation dose of 33 kGy where a broad endotherm can be observed. Effects of PLGA chain scission and localized recombination of free radicals are the most pronounced in these gamma irradiated samples. These effects lead to the increase in free volume and to the resulting polymerization products with a broad range of molecular weights. Increased chain mobility and the presence of shorter chains cause the onset of dehydration and thermal degradation events at lower temperatures.

To confirm the interpretation of DSC measurements at higher temperatures, we performed the second heating cycle with the same heating rate of 10 °C/min under nitrogen purging for the samples synthesized using gamma irradiation dose of 17 kGy and 33 kGy where the endothermic events are most pronounced at temperatures above 60 °C. **Figs. S.13** and **S.14** show the obtained DSC thermograms.

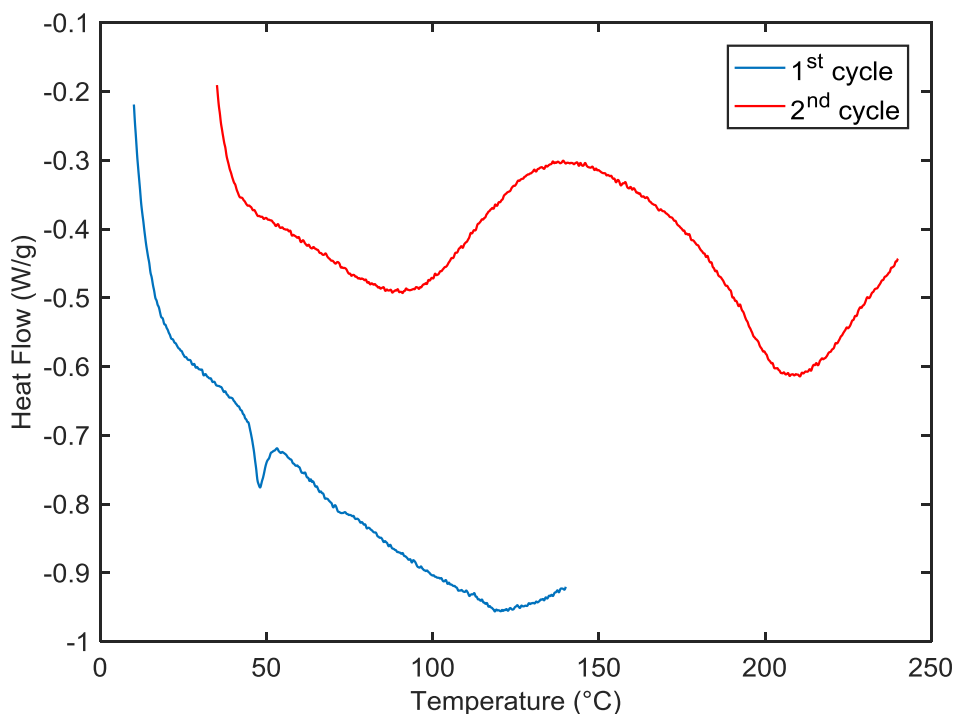


Fig. S.13. DSC thermograms of the composite PLGA-PAA hydrogel synthesized using the gamma irradiation dose of 17 kGy and dose rate of 8.1 kGy/h.

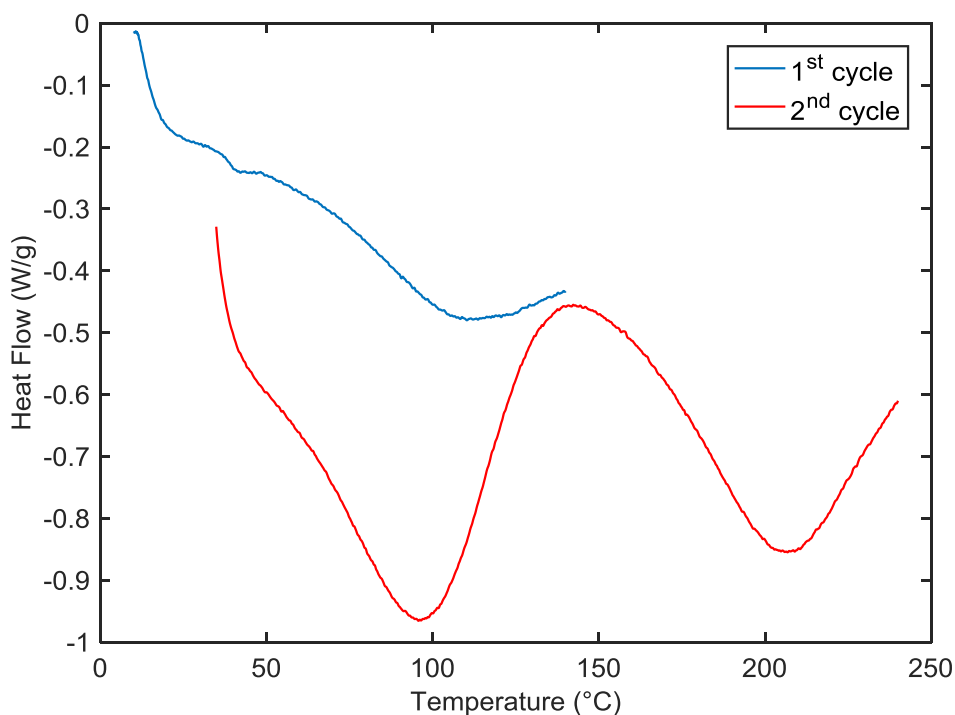


Fig. S.14. DSC thermograms of the composite PLGA-PAA hydrogel synthesized using the gamma irradiation dose of 33 kGy and dose rate of 8.1 kGy/h.

In the second heating cycle, a large broad endothermic peak appears between 60 °C and 140 °C corresponding to the increased anhydride formation. Endothermic peaks at about 120 °C disappear during the second heating cycle since the bound water was released during the first heating cycle. Similar behavior of the endothermic peak at about 125 °C was observed in the previous study (Maurer et al., 1987). Another endothermic peak appearing above 150 °C at around 210 °C corresponds mainly to the melting and thermal degradation of PLGA.

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