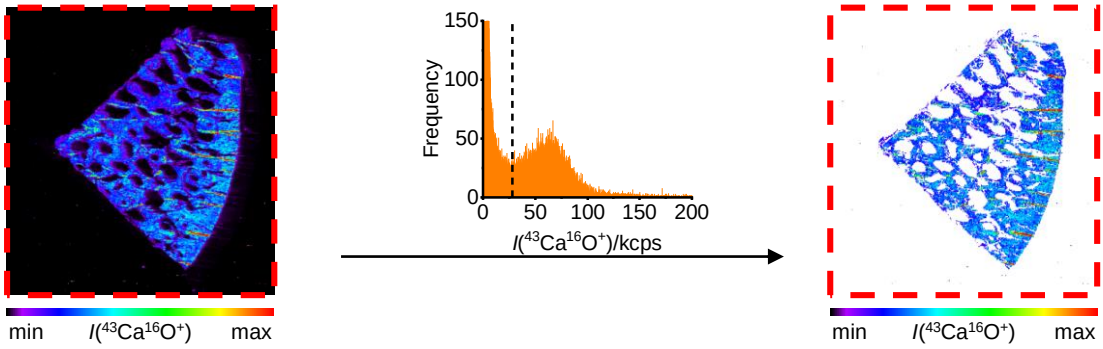
Supplemental Materials

<u>Approach to compare the gadolinium distributions in the images after exposure to different GBCAs</u>

First, a region of interest (ROI, red line) was defined. The calcium distribution, here shown as the $^{43}Ca^{16}O^{+}$ signal, was used to define the pixels containing bone material by using the respective histogram. The minimum between the distributions of signal (bone material) and noise was used as a cut off, so that only the pixels above this value were included in the further consideration.



Supplemental Figure 1: Assignment of the pixels to bone material.

As a significant portion of all pixels assigned to as bone shows gadolinium concentrations below the limit of quantification and can therefore not be used for statistical analyses, three criteria are selected to allow a comparative estimate of the gadolinium distribution in the different images:

(I) Only those pixels defined as bone material (see above) were investigated for their respective gadolinium concentrations. The concentration values of these pixels were exported, sorted from lowest to highest and the 98th percentile was determined.

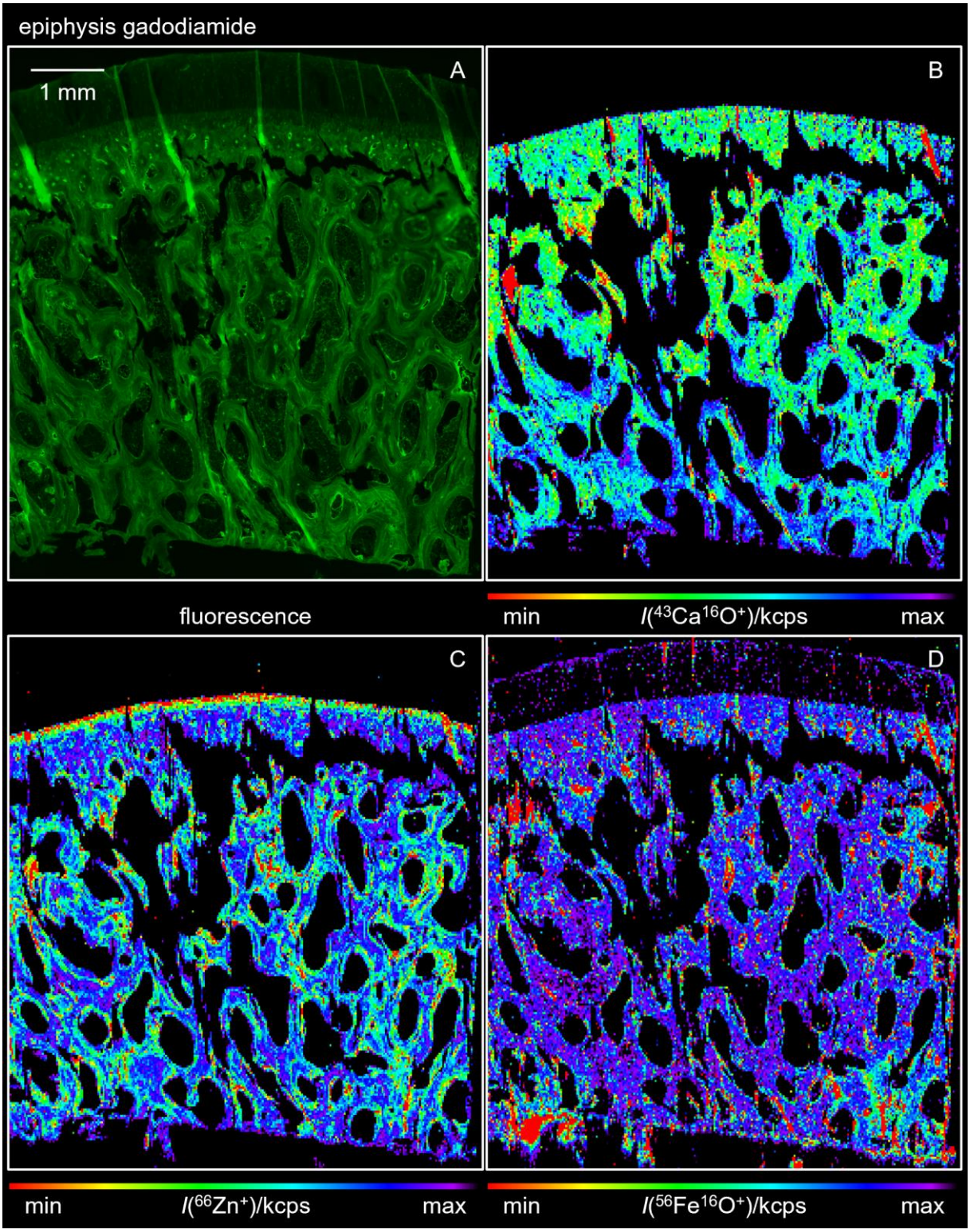
(II) Independently, the percentage of pixels among all pixels assigned as bone (see above) at or above the LOQ of gadolinium (34 ng/g) was determined for each individual image.

(III) The optical view of the image was assigned as third criterion

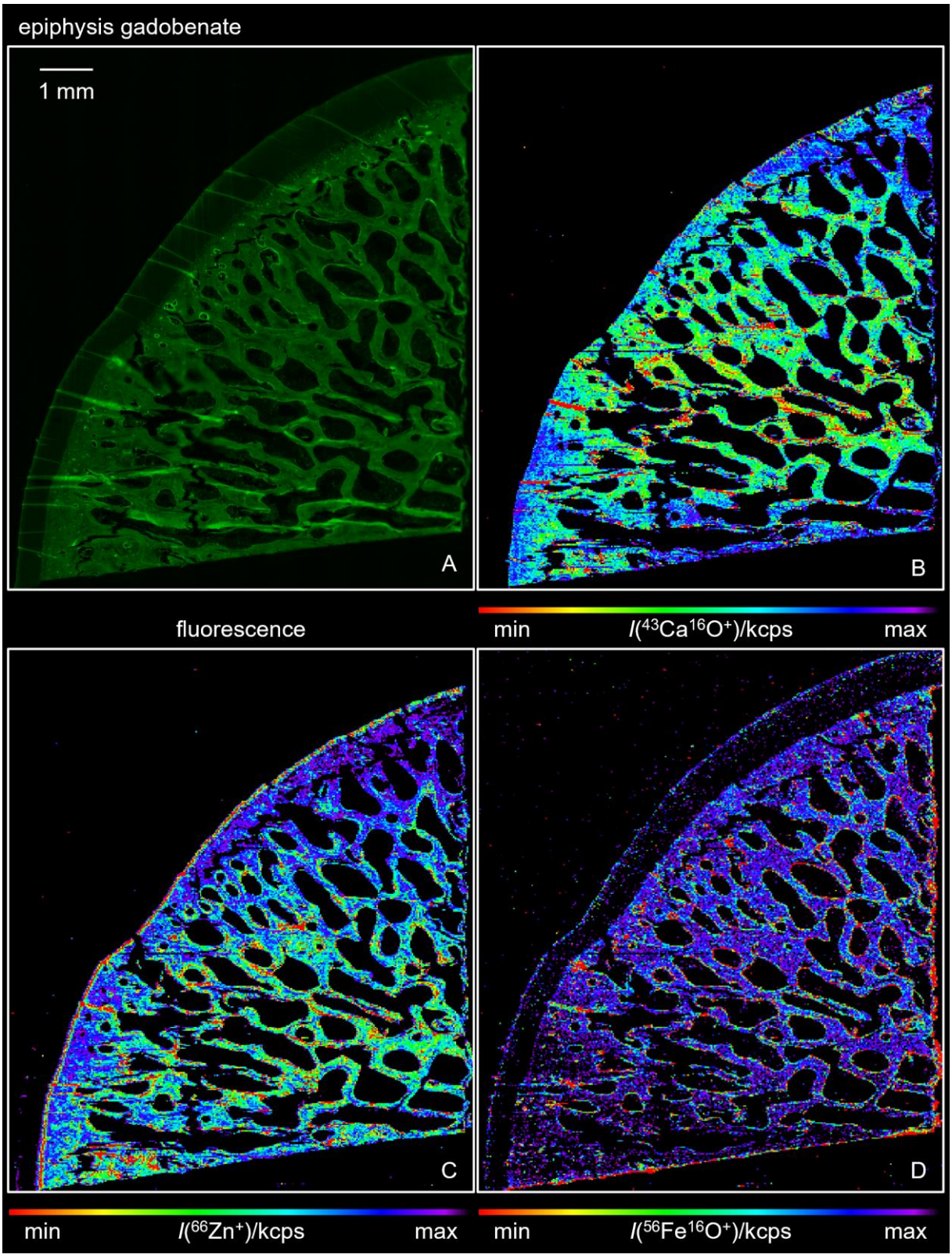
The percentile values (I), the proportion of pixels above the LOQ among the pixels belonging to the bone (II) as well as the purely optical view of the images (III) are in good agreement with each other.

Epiphysis						
GBCA	Gadodiamide	Gadobenate	Gadobutrol	Gadoteridol	Gadoterate	Saline
(I)/ng·g^{-1}	5800	720	230	92	36	<LOQ
(II)/%	94	23	13	6.8	2.3	1.2
Diaphysis						
GBCA	Gadodiamide	Gadobenate	Gadobutrol	Gadoteridol	Gadoterate	Saline
(I)/ng·g^{-1}	5100	710	400	51	65	35
(II)/%	90	21	14	2.9	4.3	2.2

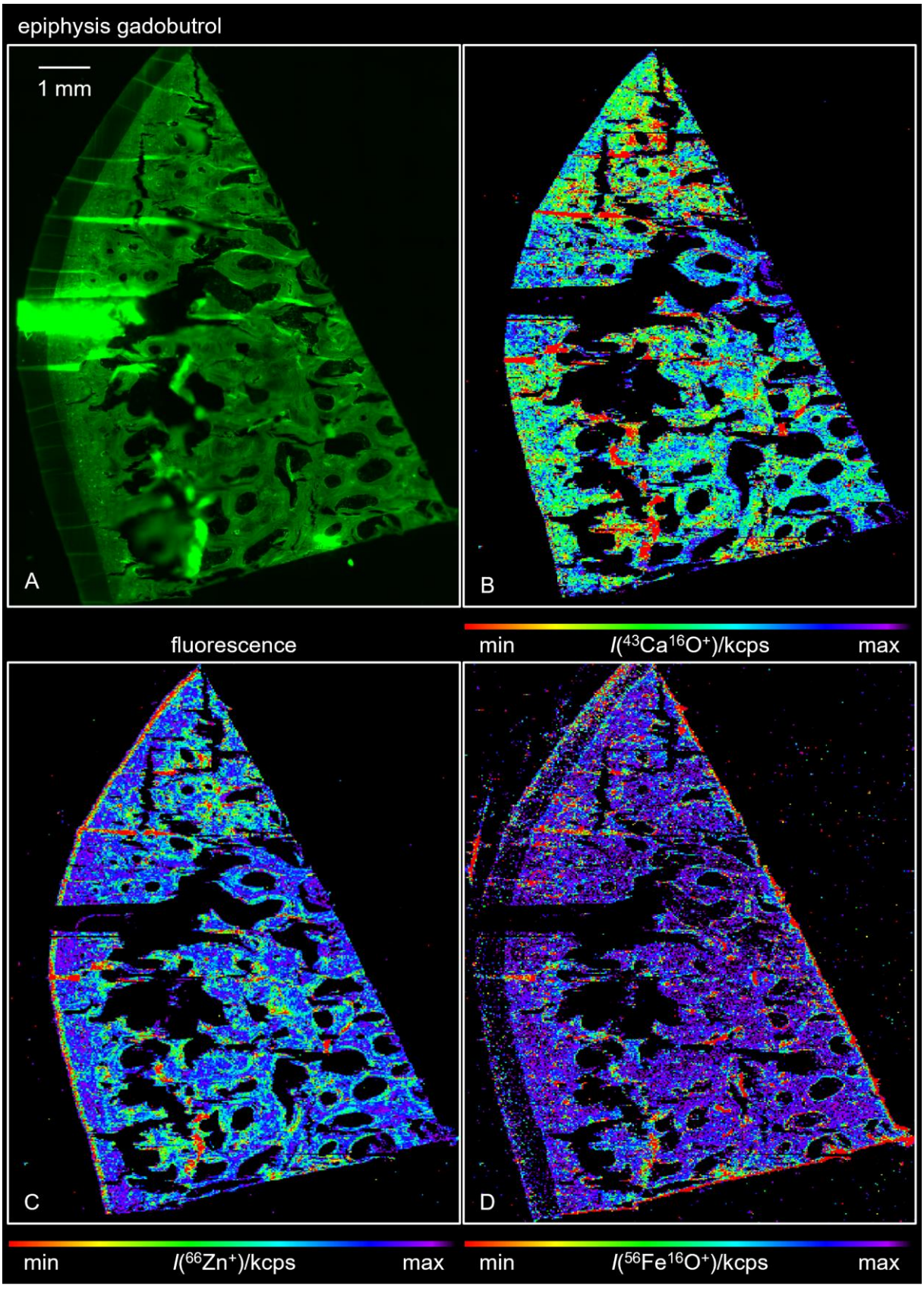
Fluorescence microscope images and elemental distributions of calcium, zinc and iron belonging to the LA-ICP-MS data shown in Figure 2



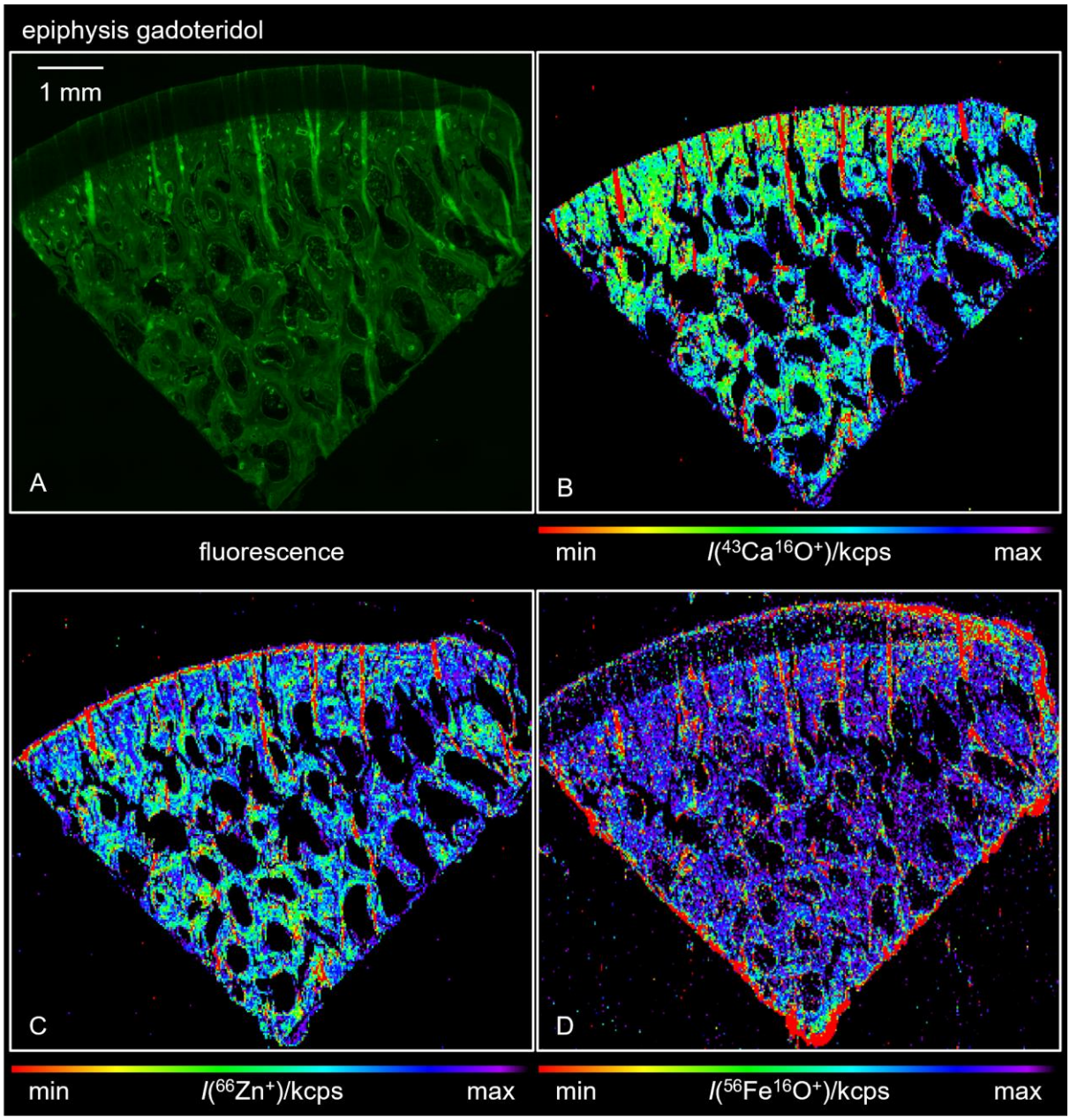
Supplemental Figure 2: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadodiamide. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



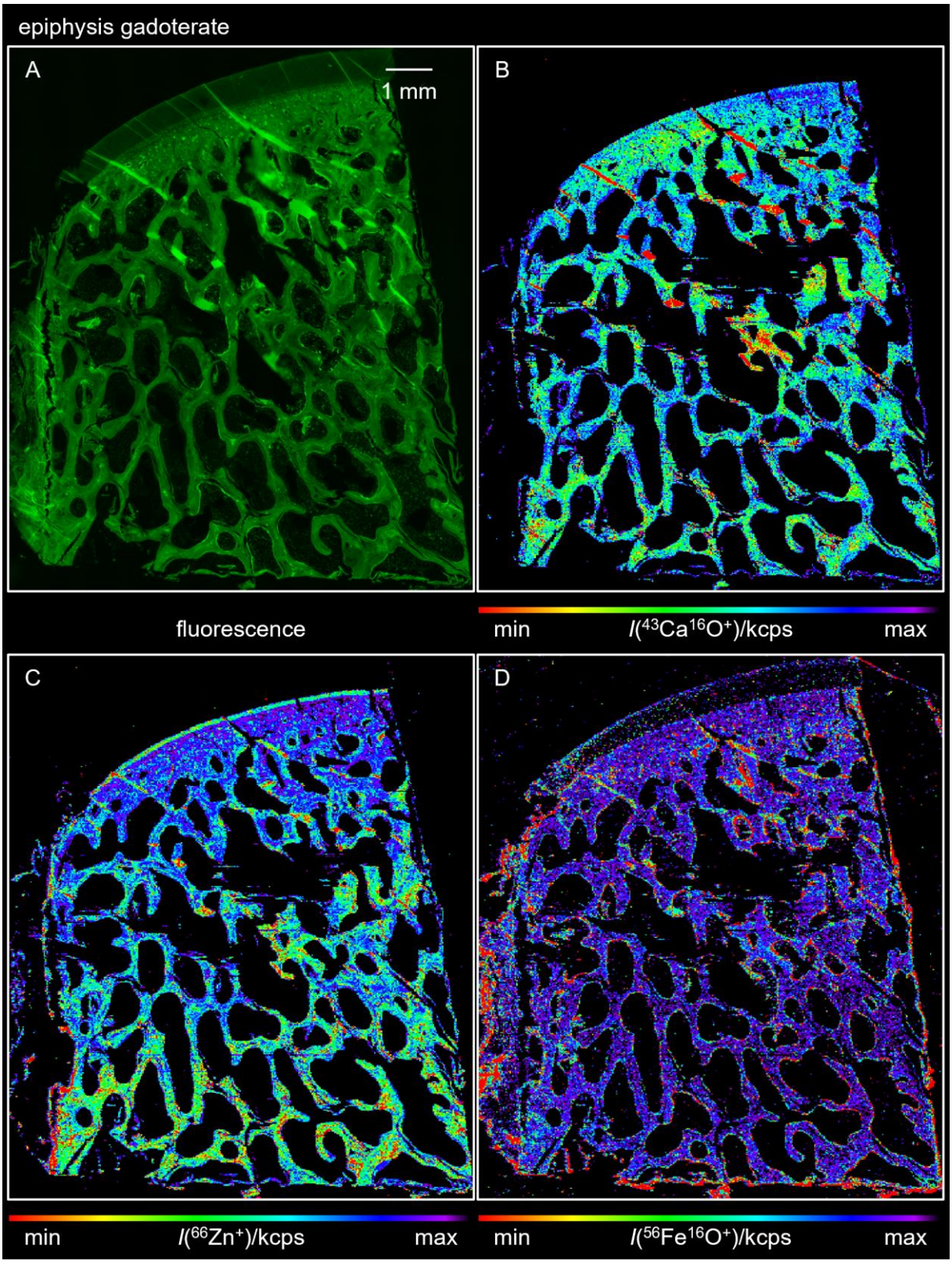
Supplemental Figure 3: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadobenate. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



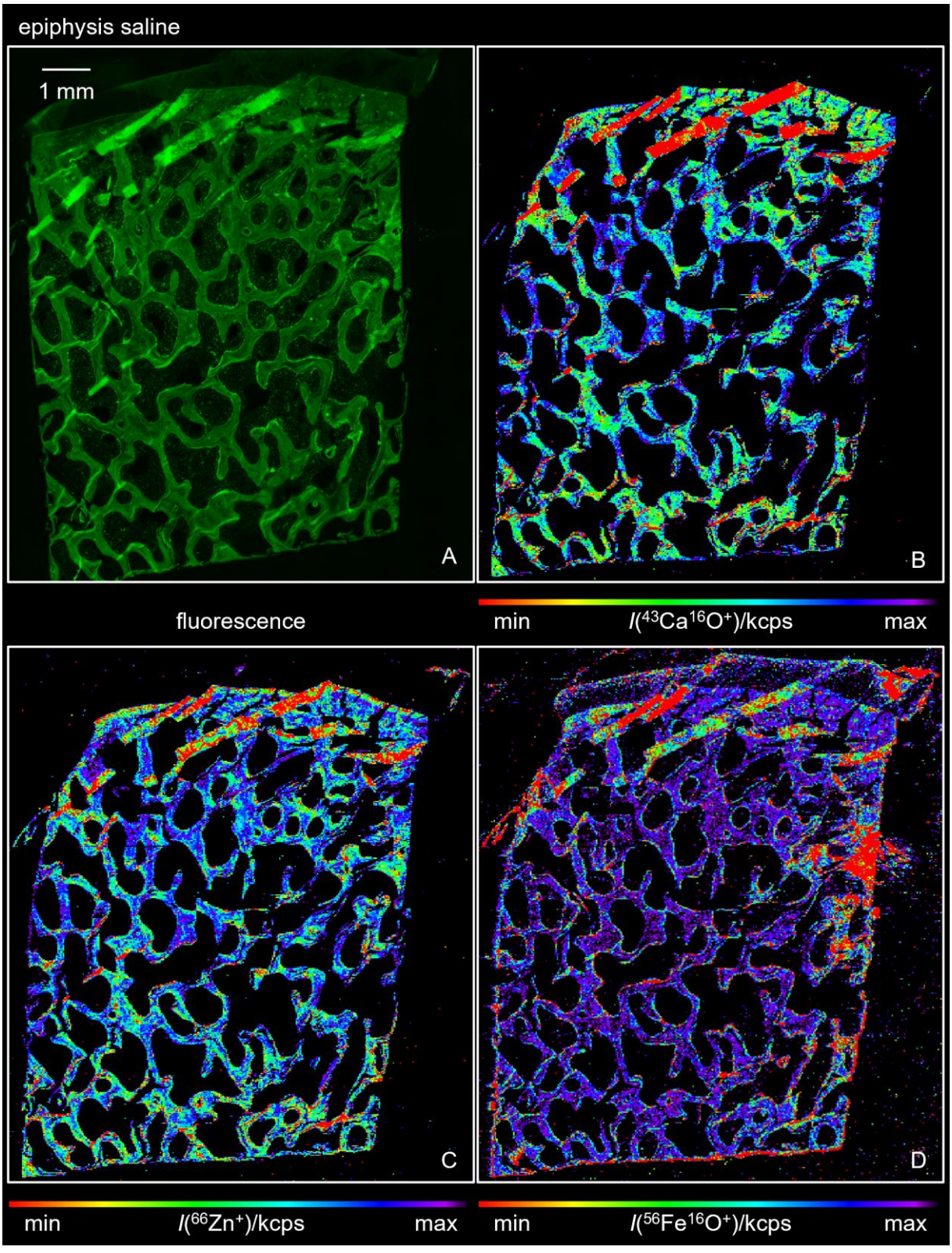
Supplemental Figure 4: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadobutrol. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



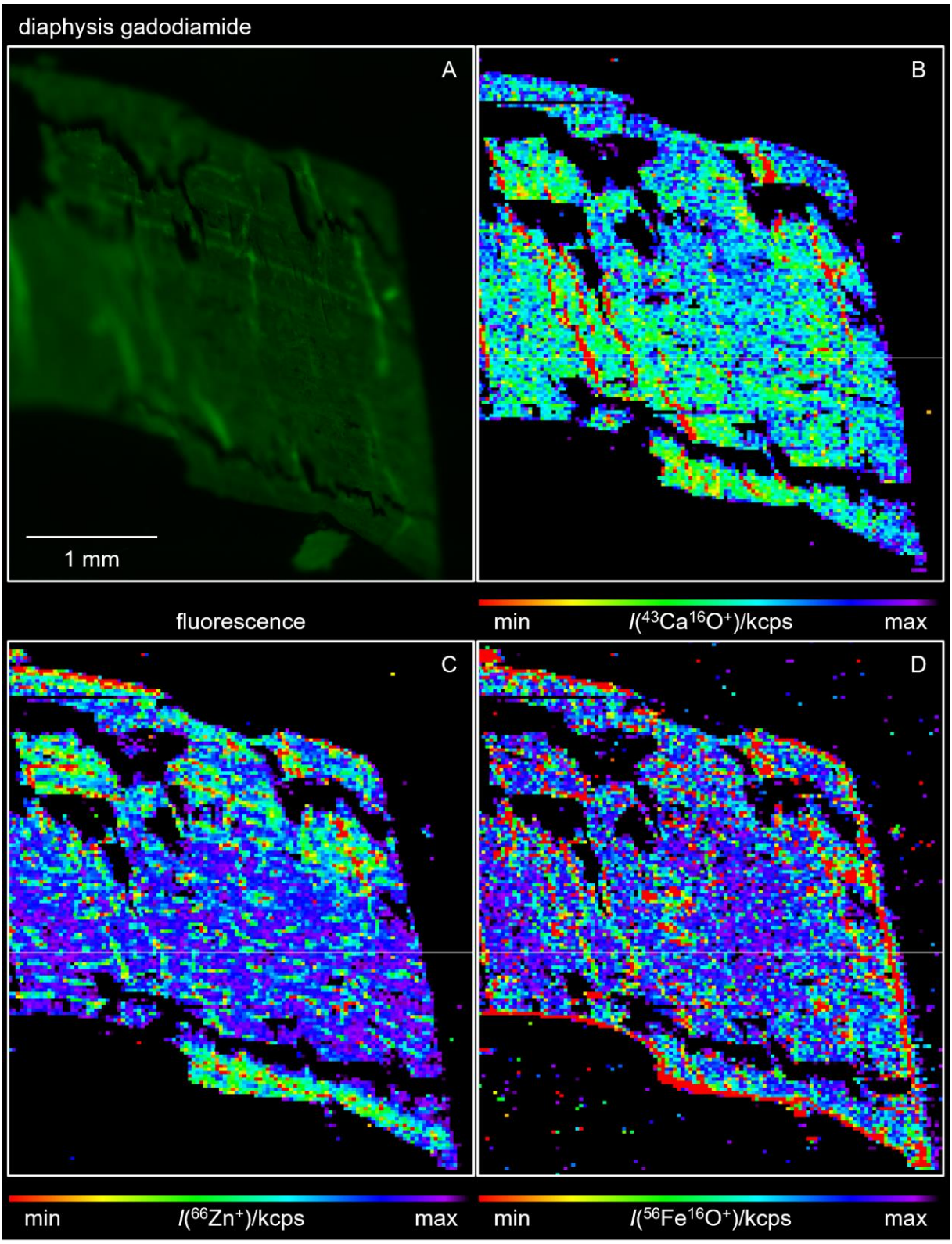
Supplemental Figure 5: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadoteridol. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



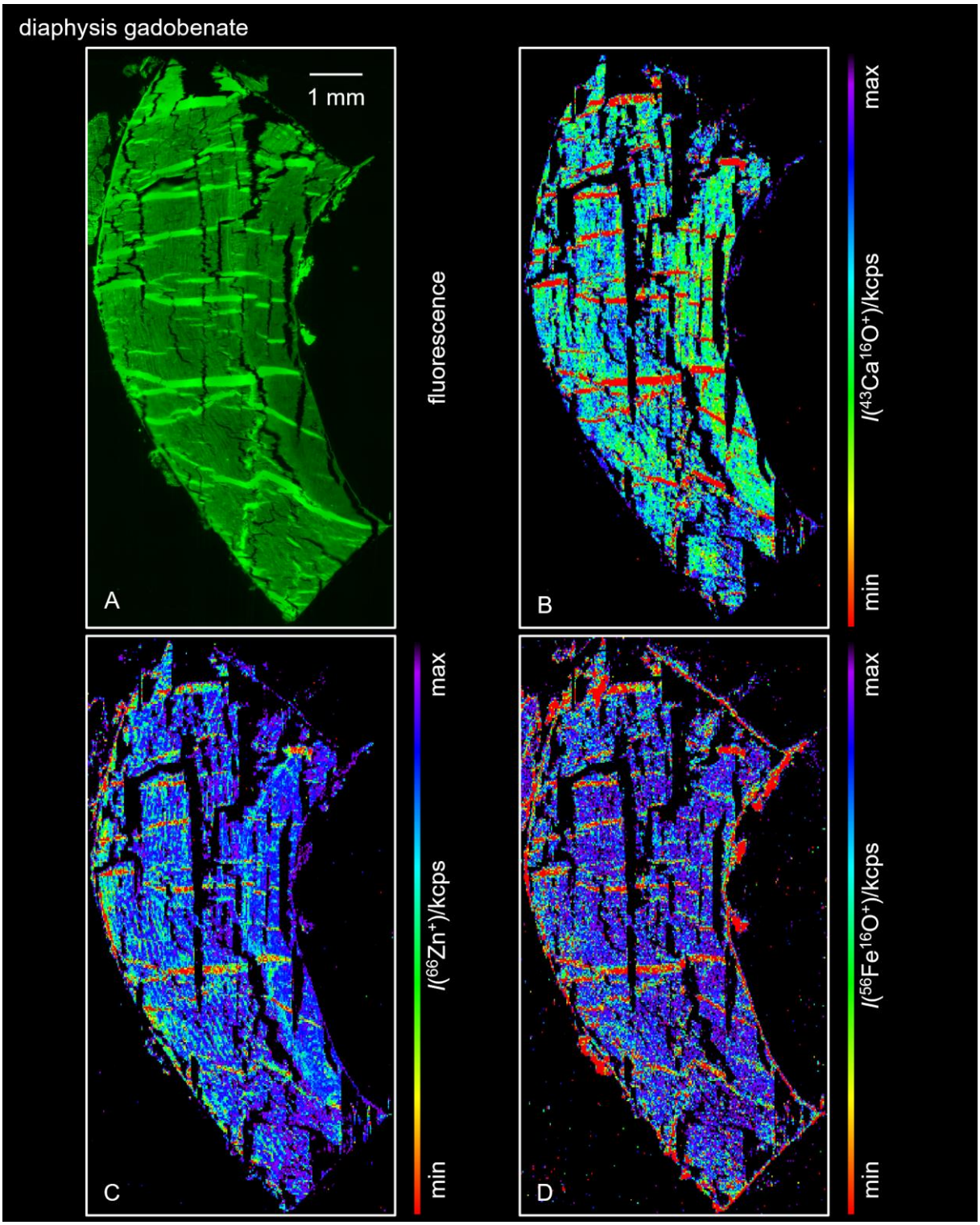
Supplemental Figure 6: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadoterate. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



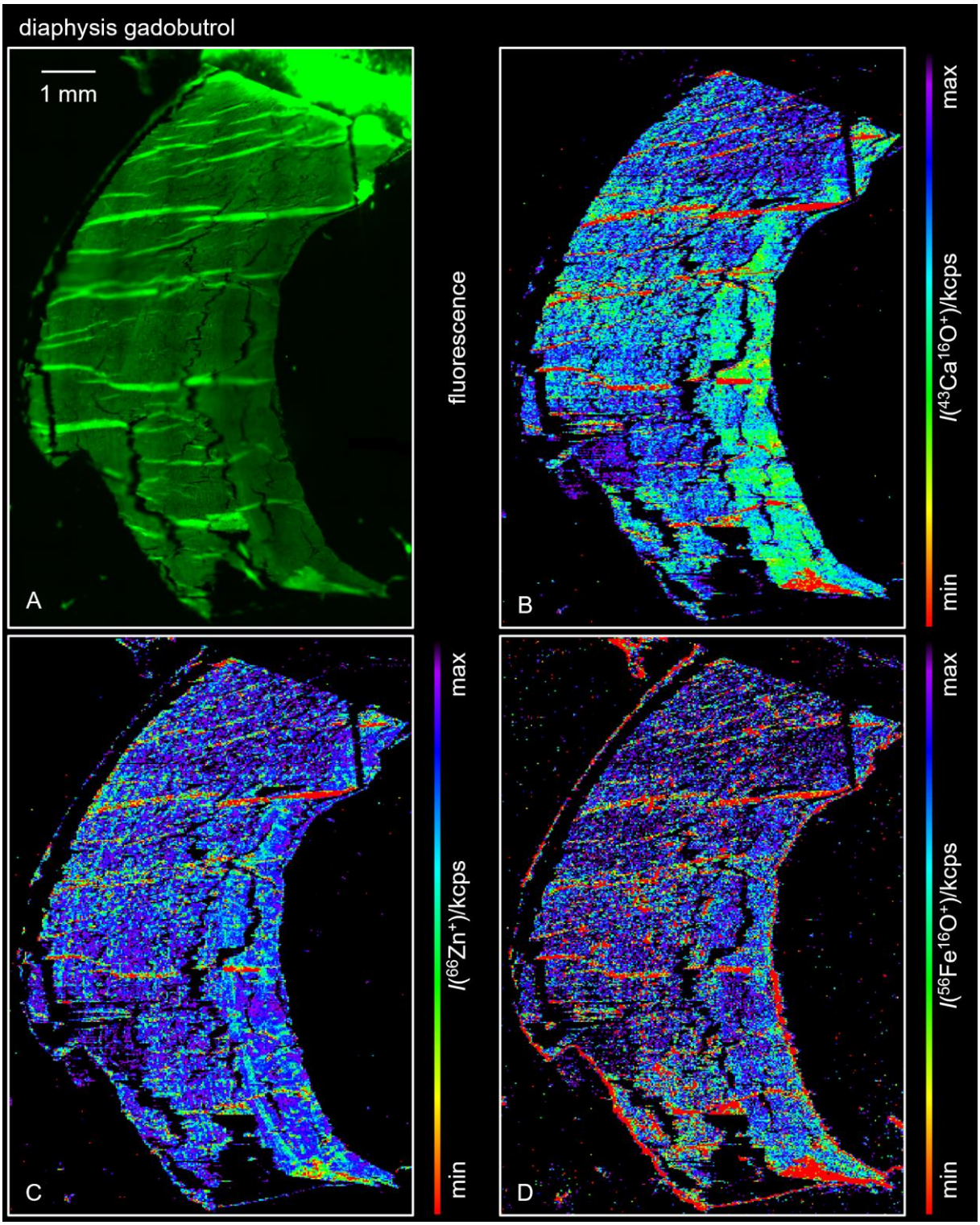
Supplemental Figure 7: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral epiphysis of a sheep ten weeks after the injection of saline. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



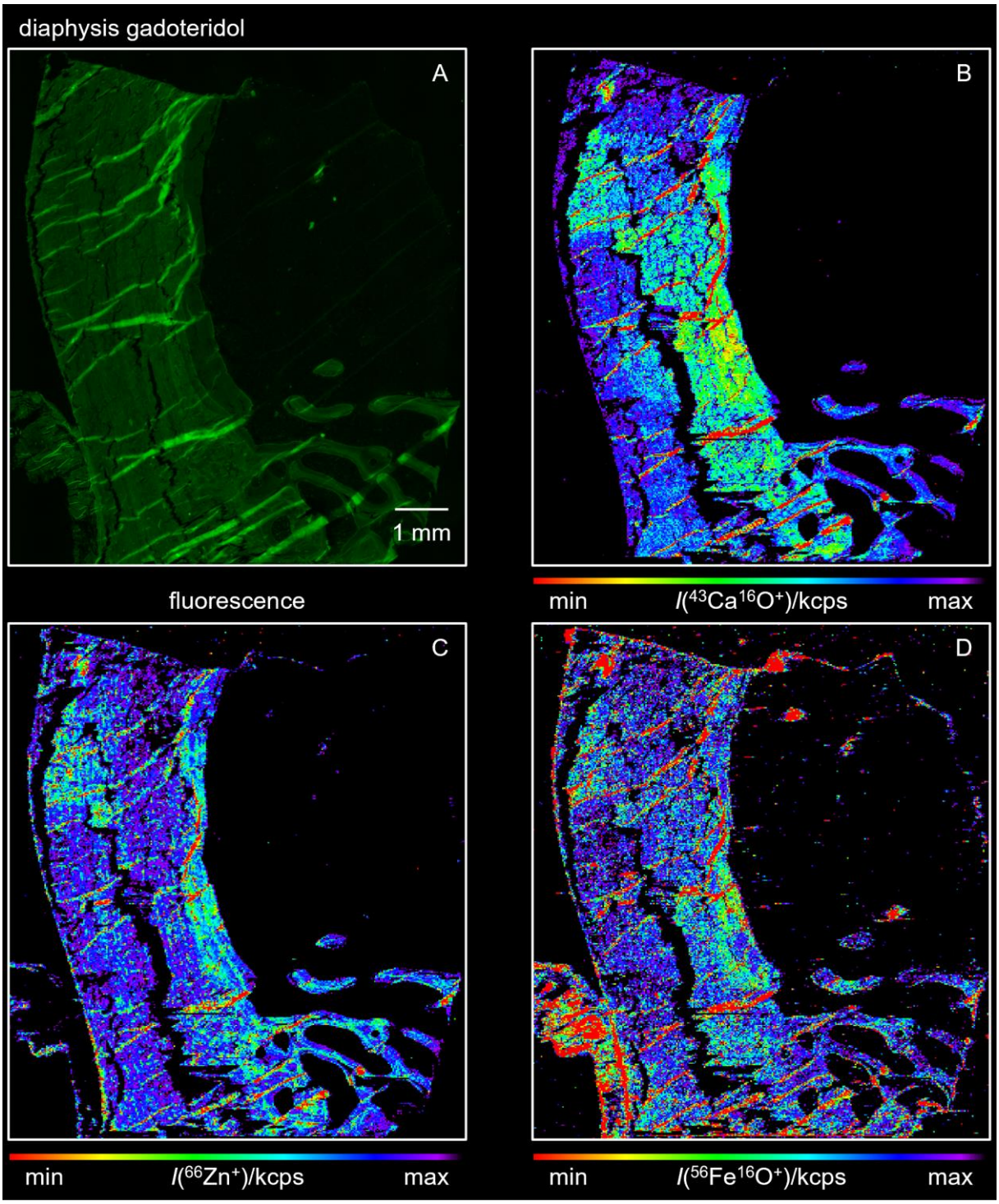
Supplemental Figure 8: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadodiamide. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



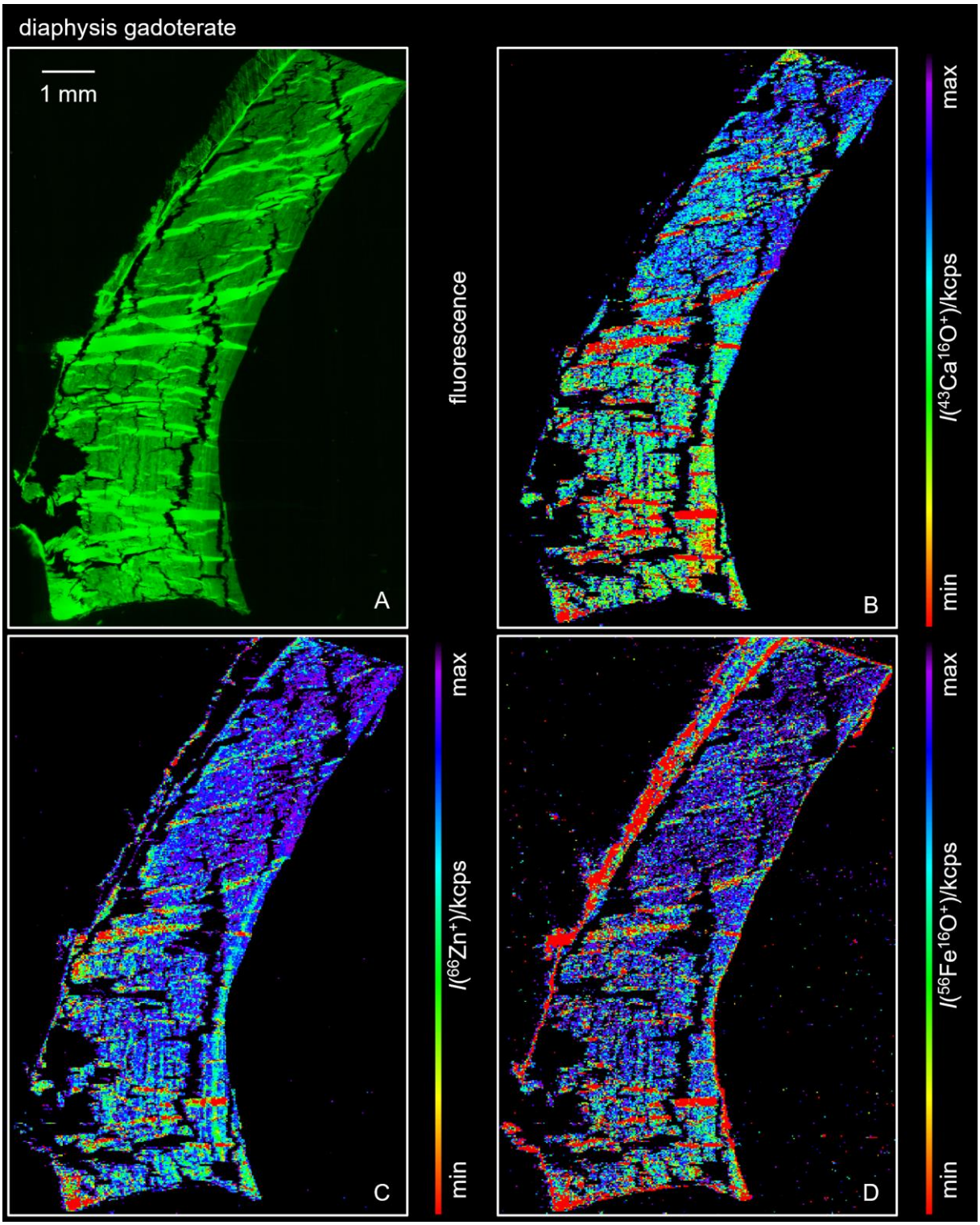
Supplemental Figure 9: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadobenate. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



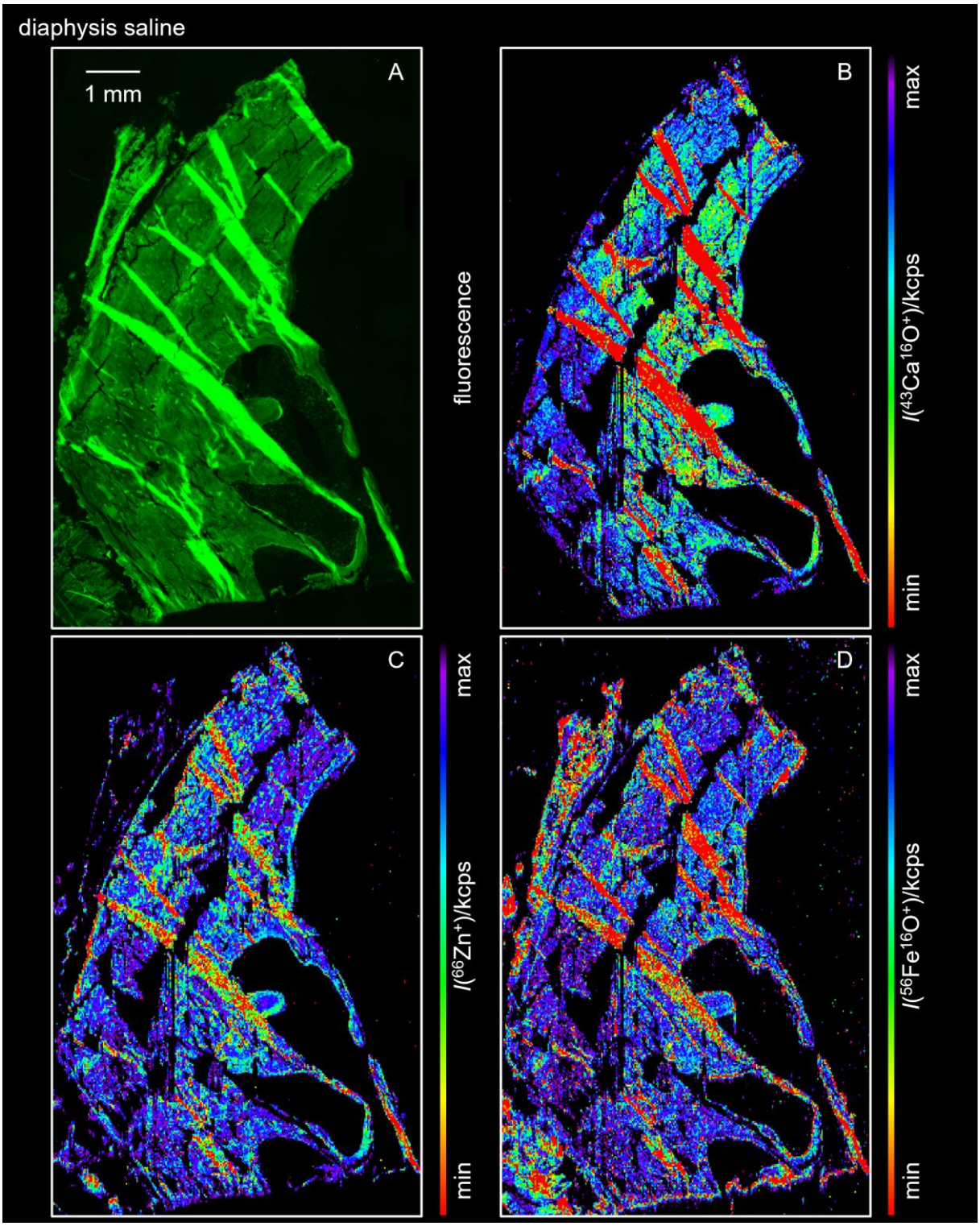
Supplemental Figure 10: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadobutrol. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



Supplemental Figure 111: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadoteridol. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



Supplemental Figure 12: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of 0.1 mmol/kg gadoterate. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).



Supplemental Figure 13: Elemental bioimaging using LA-ICP-MS with a spot size of 25 µm of a thin section from a portion of the femoral diaphysis of a sheep ten weeks after the injection of saline. Shown are the fluorescence microscope image (A) and the elemental distributions of calcium (B), zinc (C), and iron (D).