Optical tissue clearing has revolutionized researchers’ ability to perform fluorescent measurement of individual cells, protein patterning, and structural features within intact tissue samples. However, one complication common to all optically cleared tissue is a spatially inconsistent refractive index, leading to light scattering and focal plane shifts. Current methods to address this issue require highly specialized electronics and complex optics. To address the complexity and cost of current light-sheet designs for cleared tissue, we designed C-DSLM (cleared tissue digital scanned light-sheet microscopy), a simple to implement and low-cost method that automatically generates in-focus images of cleared tissue. We demonstrate the flexibility and power of the C-DSLM by quantifying fluorescent features in tissue from multiple animal models. This includes two first-in-kind measurements: 1. individual oligodendrocyte cells and myelin networks within intact optically cleared mouse brain and spinal cord and 2. vascular and neuronal networks within intact optically cleared rat eyes. For each experiment, we provide independent verification of individual cell counts and network features using standard serial tissue sectioning methods. Paired with open-source analysis tools, C-DSLM provides a robust methodology to quantify sub-micron features within large tissue sections.