



Contrast-enhanced ultrasound in children: a first-of-its-kind comprehensive compendium!

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Received: 8 April 2021 / Revised: 8 April 2021 / Accepted: 1 June 2021 / Published online: 23 July 2021
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Innovation in diagnostic imaging and interventional radiology plays an important role in the advancement and optimization of the care of our patients. Contrast-enhanced ultrasound (CEUS) is performed with the administration of ultrasound contrast agents (UCAs) and can significantly improve the conspicuity of sonographic findings and the overall diagnostic capability of ultrasound (US). This supplementary edition of *Pediatric Radiology* is devoted to the detailed presentation of CEUS, focused on its use in children.

Contrast-enhanced US has a multitude of advantages for our pediatric patients. Adding UCA to an US examination can help avoid the use of CT or MRI and thus eliminate radiation exposure or sedation/anesthesia, respectively. Other notable benefits of CEUS are the child's comfort and a positive family experience made possible by the relative ease of an US exam, including the ability to conduct the study at the bedside. The high safety profile of UCAs compared to other contrast agents, plus the fact that UCAs can be administered in children with reduced renal function, are additional important advantages of this imaging technique. However, the pivotal argument for adopting a pediatric CEUS service is diagnostic efficacy. The diagnostic value of CEUS can be comparable or even better than fluoroscopy, CT or MRI. Also, the use of UCAs allows for novel US applications that were not possible without contrast agents (e.g., intralymphatic administration), and therefore significantly widens the scope of US in children.

Since the mid-1990s, UCAs have been used off-label in children, particularly in Europe. The main application was contrast-enhanced voiding urosonography (ceVUS) for the detection of vesicoureteric reflux, and this application gradually spread to

different countries in Europe. The real breakthrough for pediatric CEUS came in 2016, when the United States Food and Drug Administration (FDA) approved the first UCA for both intravenous and intravesical indications in children. This approval was followed by subsequent pediatric approvals in Europe and China. There is no doubt that these approvals spurred the continued widespread clinical implementation of CEUS for children and prompted the expansion of pediatric CEUS research.

Considering the increasing popularity of these on- and off-label applications of UCAs, it seemed timely to publish a supplemental edition of this journal dedicated to pediatric CEUS. This comprehensive compendium on pediatric CEUS has a fourfold purpose. The first is to present all aspects of current on-label UCA applications, which include the intravenous administration for evaluation of the liver and heart as well as the intravesical use for vesicoureteric reflux detection. The second objective is to provide a detailed discussion of all current off-label applications. These comprise not only the examination of organs that are not yet approved such as the brain, but also off-label routes of administration such as intralymphatic, as well as novel uses in interventional radiology. Third, the articles in this issue review relevant CEUS applications and results in adults to underscore the pediatric applications and suggest potential future uses that can be extrapolated from the experience in adults. Last, these articles discuss both emerging pediatric CEUS applications and potential future pediatric CEUS directions. Thus, this supplement affords a most complete perspective on pediatric CEUS in the truest sense, from head to toe! We cannot think of one current subject about CEUS relevant to pediatrics that is missing in this supplement.

This supplemental edition is the result of a tremendous international collaboration. The work presented here spans more than 2 years, beginning in the pre-COVID (coronavirus disease 2019) era and struggling through the peak pandemic year 2020, but successfully emerging as planned in 2021. It covers all aspects of CEUS, with strong emphasis on pediatric CEUS in 22 publications by 205 authors. The contributions came from four continents (Asia, Europe, North America, South America)

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encompassing 15 countries (Austria, Brazil, Canada, China, Germany, Greece, Hungary, Italy, Poland, Slovenia, Spain, Sweden, United Arab Emirates, United Kingdom and United States) and 37 cities. A total of 81 unique authors from 40 institutions contributed to the pediatric CEUS supplement. It is important to note that 51 of the authors came from 18 institutions in the United States, where pediatric UCA has been approved for less than 5 years! The fact that more than 96% of the authors are pediatric imagers and researchers testifies to the widespread acceptance and use of CEUS in pediatrics. The 22 articles are not only very detailed but provide encyclopedic-like pediatric CEUS information spread over approximately 300 print pages and encompassing 210 figures with a total of 597 figure subsets, including 44 video clips in the online supplementary materials. We have incorporated 40 tables for easier overview and reference. The articles integrate a total of 1,574 references, of which 1,024 are unique for the whole supplement.

What do we hope to achieve with this compilation of pediatric-focused CEUS articles? We want to acknowledge and reinforce the central role of pediatric radiologists and other pediatric imagers in advancing pediatric CEUS. By providing a comprehensive information source in the form of journal articles, we are ensuring not only the ease of citing the articles, but also the accessibility of this important information to readers compared to a textbook or a standalone monograph on pediatric CEUS. The supplement should serve as a ready source of information on how to do pediatric CEUS and of objective evidence to justify introducing or advancing pediatric CEUS. Furthermore, the supplement serves as a thorough and reliable source for CEUS findings in different pathologies in children. It could also be used to guide future directions of pediatric CEUS research. Last, with its expansive images and videos, this journal issue and its supplementary materials can also serve as a pediatric CEUS atlas.

This work would have not been possible without the extraordinary dedication and contributions of all the authors from around the world. A million thanks to each and every one of them! Each of the manuscripts went through several rounds of reviews before being submitted, including by professional medical writers. We are immensely grateful to Lydia Sheldon, MSED, for her unwavering support with editing. We also acknowledge the support of Jennifer Wilson, who initially contributed to the editing process. We are most appreciative for the support extended to this undertaking by our multi-media specialist Jessica Yim, MS, MBA, education technology manager Brian Hopely, and special projects manager Allie Nigro, MA. Our heartfelt thanks also go to Stephanie Custer, editorial assistant for the *Pediatric Radiology* journal, for her guidance and support in the publication process. Last, we want to express our deepest gratitude to the North American editor of *Pediatric Radiology*, Dr. Peter Strouse, for his understanding, support and meticulous reviews with constructive feedback for all the manuscripts. We are grateful and honored to have been given the opportunity to serve as the editors of the first supplement on pediatric CEUS — the first for pediatric

radiology and the first of its kind. We look forward to the continued positive impact of CEUS on the care of children worldwide.

Declarations

Conflicts of interest Drs. Back and Darge have received an educational grant from Bracco Diagnostics, Inc.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



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